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CLINICAL EVALUATION OF TRANSVAGINAL MESH FOR PELVIC ORGAN PROLAPSE SURGERY

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To Stefan, Jens, Sofia and Benjamin

ABSTRACT

The objective of this thesis was to increase the understanding and assess the outcomes in terms of complications, relieve of symptoms and anatomical results of anterior vaginal wall prolapse surgery using either trocar-guided transvaginal mesh or conventional anterior colporraphy, and to identify variables associated with lateral defects.

A multicenter randomized controlled trial was performed between December 2007 and December 2008 in the Nordic countries comparing transvaginal mesh surgery for anterior prolapse with the Prolift® mesh kit with traditional anterior colporraphy. Among women undergoing the above randomized controlled trial, 50 women; 27 undergoing anterior colporraphy and 23 anterior trocar guided transvaginal mesh were examined at baseline with urodynamic assessment and at two months. We found that trocar guided transvaginal mesh of anterior vaginal wall prolapse resulting in a lowering of maximal urethral closing pressures (MUCP) and increased risk for de novo stress urinary incontinence compared to colporraphy.

A prospective multicenter cohort study was performed between June 2006 and March 2007 throughout 26 clinics in the Nordic countries. 121 patients undergoing anterior transvaginal mesh surgery was prospectively evaluated at baseline and one year after surgery using the Urogenital Distress Inventory (UDI). Overall UDI scores declined from 91 before surgery to 31 one year after surgery ($p<0.001$). UDI subscales for obstructive and irritative symptoms improved one year after surgery ($p<0.001$ for both) while stress symptoms did not ($p= 0.11$).

In a subanalysis from the randomized controlled trial of mesh kit versus anterior colporraphy 99 patient were included diagnosed at baseline with a lateral defects in the anterior vaginal wall. 39 patients underwent anterior colporraphy and 60 anterior trocar guided transvaginal mesh surgery and one year after surgery, a persistent lateral defect was significantly more common after colporraphy compared to transvaginal mesh (11/32 (34.4%) vs 1/42 (2.4%), risk ratio 14.4 (95% CI 2.0-106.1) ($P<0.001$).

To determine variables associated with lateral defects a cross-sectional study was performed as subanalysis of a multicenter, randomized, controlled trial. 99 patients classified as having a lateral defect and 203 patients with isolated central defect of the anterior vaginal wall were compared with regard to clinical characteristics and urogenital distress. Among the investigated patient characteristics, only hormone replacement therapy (HRT) use at baseline was associated with lateral defects (OR 2.7, 95% CI 1.2-6.3) whereas previous anterior vaginal wall repair decreased the odds for lateral defects (OR, 0.3, 95% CI 0.1-0.9) in a multivariable model. Patients with lateral defects experienced more symptoms of bulging compare with patients without lateral defects ($p=0.02$).

In conclusion, the four studies in the thesis have shown that transvaginal mesh for anterior pelvic organ prolapse provides satisfactory anatomical and subjective outcome. However, there is an increased risk of problems with stress urinary incontinence after mesh surgery. In comparison with traditional surgery, prolapse surgery with mesh still is a new method with potential risks and benefits, especially in the long term, and must be carefully considered.

LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to by their Roman numerals:

I Ek M, Tegerstedt G, Falconer C, Kjaeldgaard A, Rezapour M, Rudnicki M, Altman D
Urodynamic assessment of anterior vaginal wall surgery: a randomised comparison between colporraphy and transvaginal mesh
Neurourology and Urodynamics, 2010;29(4):527-31

II Ek M, Altman D, Falconer C, Kulseng-Hanssen S, Tegerstedt G
Effects of Anterior Trocar Guided Transvaginal Mesh Surgery on Lower Urinary Tract Symptoms
Neurourology and Urodynamics, 2010;29(8):1419-23.

III Ek M, Altman D, Gunnarsson J, Falconer C, Tegerstedt G
Clinical efficacy of a trocar guided mesh kit for the repair of lateral defects
Submitted

IV Ek M, Altman D, Falconer C, Hammarström M, Tegerstedt G
Clinical characteristics and symptoms in relation to lateral defects among women with anterior vaginal wall prolapse
Manuscript

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1 LIST OF ABBREVIATIONS

POP	Pelvic Organ prolapse
POP-Q	Pelvic Organ prolapse Quantification
BMI	Body Mass Index
SUI	Stress Urinary Incontinence
TVM	Transvaginal Mesh
OR	Odds Ratio
RR	Risk Ratio
CI	Confidence Interval
ICS	International Continence Society
UDI	Urogenital Distress Inventory
Aa	Point A on anterior wall
Ba	Point B on anterior wall
C	Cervix or cuff
FDA	Food and Drug Administration
TVM	Transvaginal mesh
SD	Standard Deviation
TVT	Tension free vaginal tape
MUCP	Maximal Urethral Closing Pressure

2 INTRODUCTION

Pelvic organ prolapse (POP) is characterized by a downward descent of the pelvic organs, causing the vaginal walls or the uterus, or both to protrude. (1) Pelvic organ prolapse is a common condition affecting millions of women worldwide. In the United States alone, more than 300,000 surgeries for pelvic-organ prolapse are performed each year, of which anterior colporrhaphy for prolapse of the anterior vaginal wall (cystocele) is the single most common operation. In Sweden, 8,700 surgical procedures for pelvic organ prolapse were performed in 2010 (www.socialsyrelsen.se/statistik).

POP is a condition which affects all aspects of daily function and quality of life. (2) Surgery remains the mainstay of treatment for POP but it is increasingly recognized that traditional surgical procedures often are associated with unsatisfactory outcomes. Because the risk of recurrence is 40% or more with traditional procedures, (3-5) there has been great interest in innovative surgical techniques that may improve outcomes after POP repair. Yet the evaluation of complex interventions has not kept pace with the rapid development of novel invasive therapies that involve synthetic implants. Several observational studies have shown lower failure rates after biomaterial-augmented surgery, as compared with the traditional repair of POP, but data from randomized trials to support specific treatment recommendations have been lacking.

Standardized trocar-guided mesh kits represent the most recent development in the field of POP surgery. Mesh kits procedures are increasingly used in prolapse surgery, and the approach differs fundamentally from traditional POP repair. These operations involve the use of metal trocars for placement of a synthetic mesh, which is standardized in shape and size, to support the vaginal walls. Similar to the situation for ordinary mesh, clinical data on the safety and efficacy of mesh kits have been scarce and long-term outcomes are practically unknown. The main objective of this thesis was to assess clinical outcomes after anterior vaginal wall prolapse surgery using either trocar-guided transvaginal mesh.

3 BACKGROUND

3.1 Anatomy

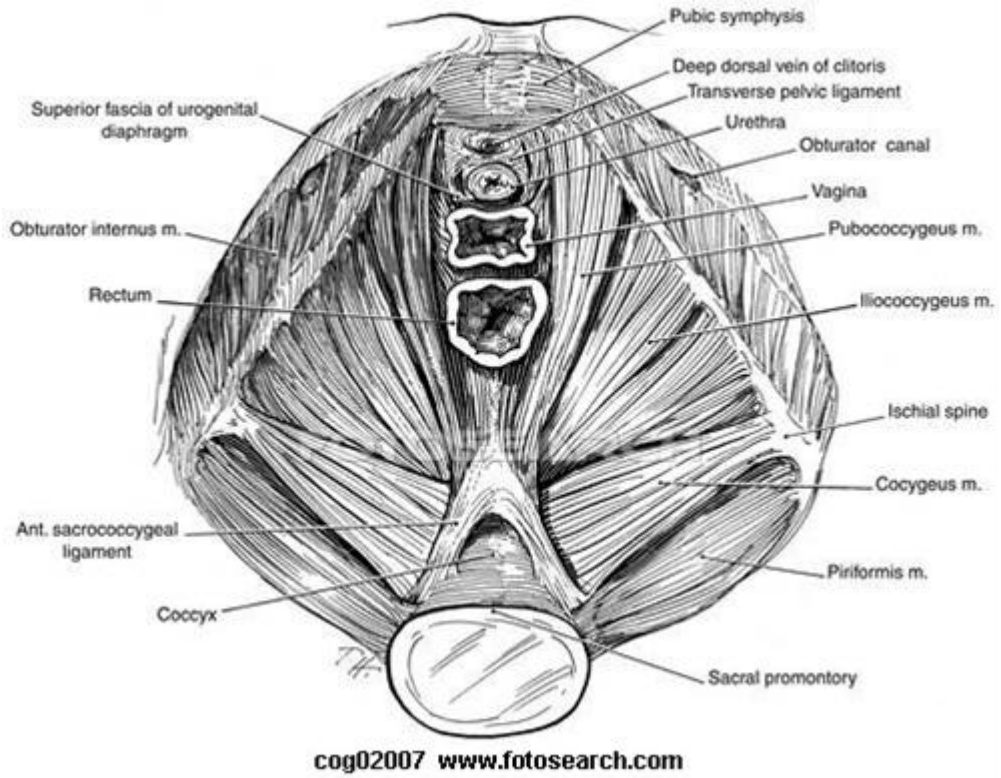
3.1.1 The female pelvic floor

The pelvic floor consists of muscular and connective tissues which prevent the female pelvic organs from being pushed out by intra-abdominal pressure. The pelvic floor also has important functions relating to sustaining urinary and fecal continence, sexual function and reproduction.

3.1.2 The pelvic diaphragm

The levator ani muscle consists of the iliococcygeus muscle, pubococcygeus (pubovisceral) muscle and the puborectal muscles. Together with the coccygeus muscles, the endopelvic fascia, smooth muscles and connective tissue it forms the pelvic diaphragm (Figure 1). The pubococcygeus muscles are directly attached to the bladder, urethra, vagina and rectum and actively contribute to visceral control. These muscles are contracted at rest and act to close the genital hiatus to provide a platform for the pelvic organs. The puborectal muscle forms a sling around and behind the rectum. The endopelvic fascia is a sheet of connective tissue which surrounds the vagina and attaches the vaginal wall to the pelvic arcus tendineus fascia laterally.

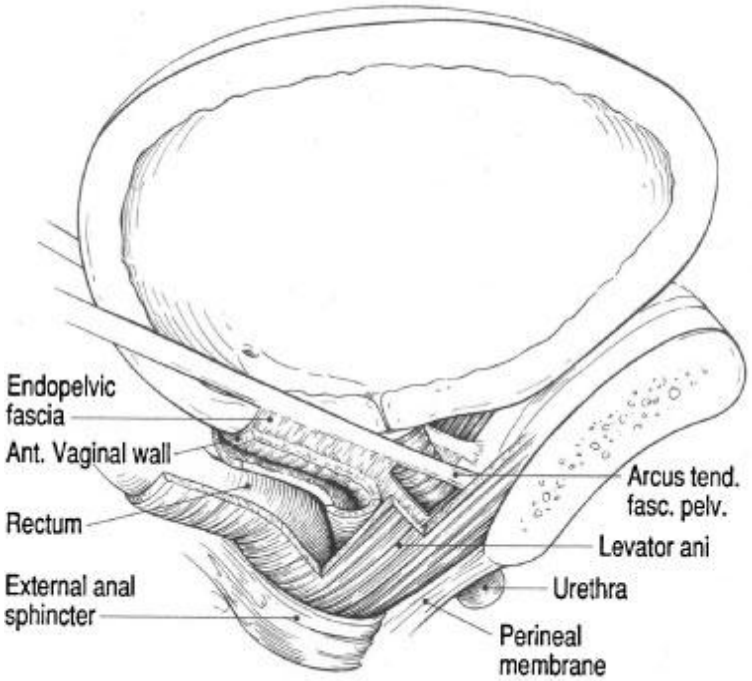
Figure 1. Pelvic floor, seen from above, the pelvic musculature resembles a concave plate.



3.1.3 The lateral pelvic support and urethral support structures

A linear condensation of the obturator and levator ani fascia forms the arcus tendineus fascia pelvis (ATFP) – a fibrous band extending from pubic bone to the ischial spines. The ATFP is a supporting structure of the pubocervical and rectovaginal fascia. The major components of the urethral supportive structure are the vaginal wall, the endopelvic fascia, the ATFP, and the levator ani muscles (Figure 2). During cough, the levator ani muscle contracts simultaneously with the pelvic diaphragm and abdominal wall muscles to build abdominal pressure. The levator ani contraction helps to tense the suburethral fascial layer, thereby increasing urethral compression. (6-8)

Figure 2. Lateral view of the components of the urethral support system.



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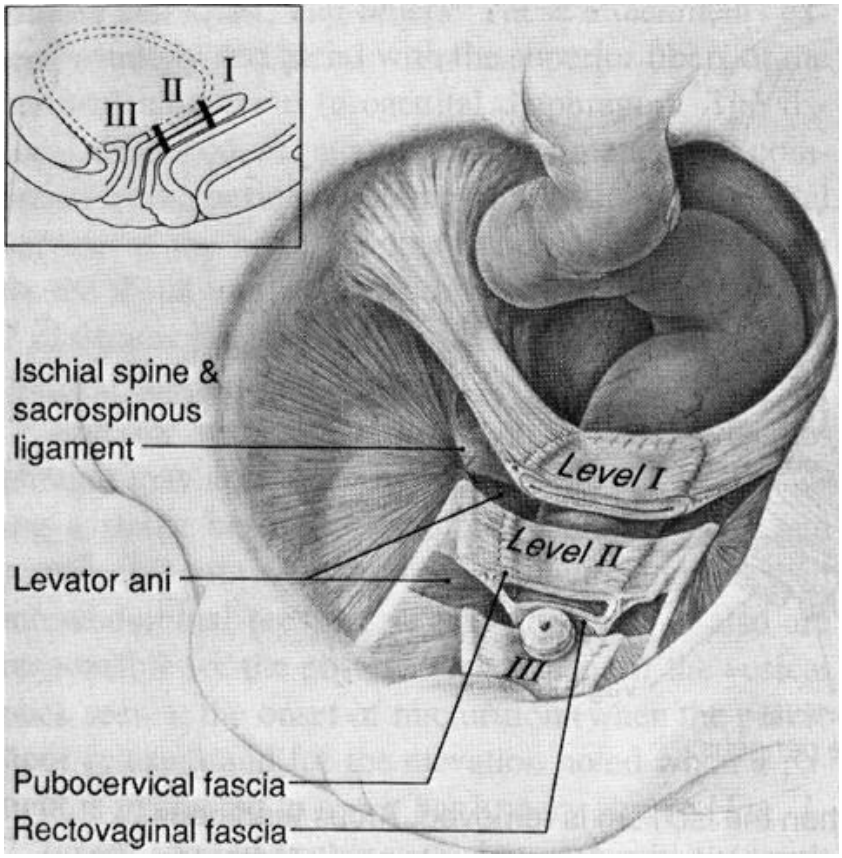
3.1.4 Levels of vaginal support

In 1992, DeLancey presented a description of anatomical levels of support for the vagina (Figure 3). (9) According to DeLancey the vagina has three levels of support: Level I suspends the upper third of the vagina and relies primarily on the uterosacral and cardinal ligaments; Level II is the middle third of the vagina and is suspended by the arcus tendineus fascia pelvis, pubocervical fascia and rectovaginal fascia; and the distal support at Level III which includes the pubocervical and rectovaginal Fascia, the pubourethral ligaments and perineal body. Deficiencies at any of the described levels will result in isolated, or combinations of, POP. For example, loss of level I support will result in uterine prolapse if the uterus is intact or vaginal vault prolapse if the uterus has been removed.

Figure 3. Levels of vaginal support.



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Level I:
The upper third of the vagina. The Uterosacral and Cardinal ligaments.

Level II:
The middle third of the vagina. Arcus Tendineus Fascia Pelvis. Pubocervical and Rectovaginal Fascia.

Level III:
Pubocervical and Rectovaginal Fascia (Distal) Pubourethral Ligament and Perineal Body.

3.1.5 Pelvic floor defects

The anatomic origin of POP can be viewed as a deficiency in three different compartments; the anterior, posterior and the apical compartment. The section below provides a brief summary of defects in the anterior compartment as described at the 2011 ICS. (10)

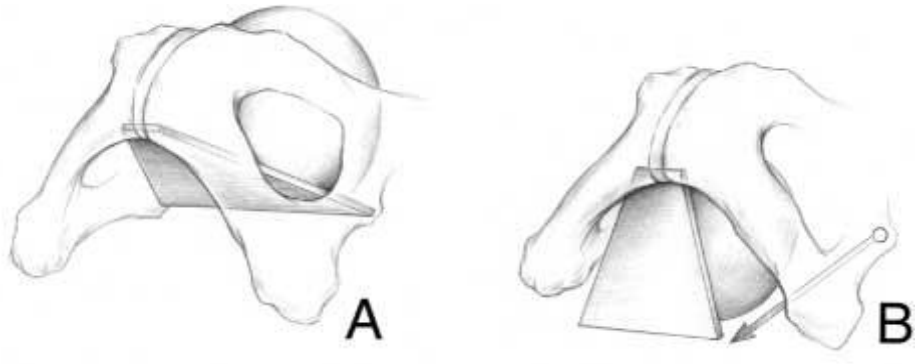
1) The lateral (paravaginal) defect occurs when the anterior vaginal wall and pubocervical fascia has dislodged from its lateral attachment to the ATFP on one or both sides (Figure 4). This involves a level II defect.

2) The transverse defect is a separation of the pubocervical fascia from its attachment to the pericervical ring of tissue at the apex of the vagina.

3) The central defect is any break in the pubocervical fascia upon which the bladder is resting.

4) Distal defect (urethrocele) involves a herniation of the fascia supporting the distal urethra.

Figure 4. Lateral defects



The attachments of the ATFP to the pubis and the ischial spines are intact (A). The connection to the spine has been lost, allowing the fascial plane to swing downward (B). (Reprinted with permission from JOL DeLancey).

3.2 Epidemiology

Pelvic organ prolapse is one of the most common indications for gynecological surgery but population-based epidemiological studies of the incidence and prevalence of this disorder are rare. (1, 11) Pelvic floor defects in women presenting for routine gynecological visit is seen in 43-76% of patients, with 3-6% having descent beyond the hymen. (12) In a cross-sectional study of 27,342 women age 50-79 years who underwent pelvic examination, 41% of women showed some degree of pelvic organ prolapse. (13) In Sweden, the prevalence of symptomatic POP has been estimated to range between 8.3% and 15%. (11, 14)

A woman's lifetime risk of surgery for pelvic organ prolapse by age 80 years is about 7%. (15) The peak incidence of POP surgery occur women aged 50-65 years. (11, 16) An estimated 13% of patients who have surgery will need a repeat operation within 5 years. (15, 17, 18)

3.3 Ethiology and risk factors

The underlying ethiology of POP is multifactorial and many risk factors have been suggested. (19) The most consistent risk factors are vaginal childbirth, advancing age, obesity and family history. (1, 20) Vaginal birth increases the risk of POP by 4 to 11 times (21) and stress urinary incontinence by 2.7 times (22) and multiple deliveries increases the risk for symptomatic POP. (23) Magnetic resonance imaging (MRI) and ultrasound studies have demonstrated levator ani muscle defects after childbirth (24, 25) and their association with POP and SUI. (26-28) Decline of normal levator ani tone, by denervation or direct muscle trauma, results in a widened urogenital hiatus and weakening of the levator plate. DeLancey et al. found that women with POP had an odds ratio of 7.3 for having major levator ani defects at MRI compared to women without prolapse. (27) Also other environmental risk factors have been identified such as occupations which entails heavy lifting (29), chronic constipation (30) and genetic factors. (31) Hysterectomy might increase the risk of subsequent POP but development of symptomatic prolapse happens many years after this procedure. (15, 21, 32)

Changes in endogenous collagen metabolism and reduced collagen content are considered an important contributing mechanism to POP. (33, 34)

3.4 Symptoms

There are several symptoms associated with POP but the most specific is "seeing" or "feeling" a vaginal bulge. (1, 3, 35, 36) Other symptoms associated with POP includes bladder, bowel but the correlation with organ specific dysfunction is moderate. (35, 37) Ellerkman et al. assessed 237 women with symptomatic POP and found that 63% reported bulge symptoms, 73% urinary incontinence, 86% urinary urgency or frequency, 62% voiding dysfunction and 31% fecal incontinence. (35) Only weak-to-moderate correlations have been described between prolapse stage and presence of prolapse symptoms. (18, 35, 38, 39) The hymen seems to be an important cut-off point as women with prolapse beyond the hymen have more pelvic floor symptoms and are more likely to report a vaginal bulge than women with prolapse at or above the hymen. (12, 35, 37, 40) However, Barber et al analyzed data from 322 women with POP and paradoxically 17% of subjects in this population who reported vaginal bulge symptoms demonstrated good anatomic support (stages 0 or 1). (38)

3.4.1 Urinary symptoms and prolapse

According to the report from the ICS 2002 lower urinary tract symptoms are divided into three groups: storage, voiding, and post micturition symptoms. Storage symptoms include increased frequency, nocturia, urgency and urinary incontinence (stress-, urge and mixed incontinence). (41) POP and lower urinary tract symptoms often occur together. (42) (3) In a review article, the prevalence of stress urinary incontinence (SUI) in patients with POP range between 13-83% . (43) SUI particularly co-exist with POP when the prolapse is mild. (40) Women with POP extending beyond the hymen are less likely to report SUI which may be due to mechanical obstruction of the urethra. (39) Romanzi et al. reported that urinary obstruction occurred in 58% of women with grade 3 and 4 anterior wall prolapse compared with 4 % in women with grade 1 and 2 prolapse. (44)

Richardson et al. observed that loss of anterior wall descent occurred because of lateral detachment rather than midline stretching in women with SUI and urethral hypermobility. (45) DeLancey et al. found that detachment of the arcus tendineus fascia pelvis (ATFP) from the spine is associated with anterior vaginal wall prolapse and may affect urethral support and SUI. (46, 47)
The prevalence of women with POP who complain of urge urinary incontinence ranges between 21-73% in different studies. (43) The relationship between the grade of prolapse and symptoms such as urgency and urge incontinence has been inconsistent in existing studies.

3.4.2 Occult urinary incontinence

Occult stress incontinence is defined as incontinence masked by POP in which bladder obstruction due to kinking or compression may prevent urinary leakage. (48) POP surgery may therefore relieve the obstruction with the result of postoperative SUI in previously continent patients. After POP surgeries, without concomitant anti-

incontinence surgery, between 13% to 67% of patients develop de novo incontinence. (49-52) In a 2011 Cochrane review, 187/1280 women (15%) reported de novo stress urinary incontinence after prolapse surgery. De novo overactive bladder symptoms were noted in 103 /854 (12%) women. (53)

3.4.3 Prolapse reduction tests

Rates of urodynamic stress incontinence with prolapse reduction reported in symptomatically continent women with prolapse range from 25-100%. (48, 54, 55) (56-58) In the Colpopexy and Urinary Reduction Efforts (CARE) trial they compared five methods of prolapse reduction in detecting occult urodynamic stress incontinence (Table 1). (51) Overall, the prolapse reduction tests had a low sensitivity (5-39%) and high specificity (74-96%). They found that the ability to predict postoperative incontinence to be variable among the five methods and the pessary prolapse reduction test to be least predictive one (50%) and the cotton swab test had the highest positive predictive value (79%).

Table 1. Rates of urodynamic stress incontinence with various methods of prolapse reduction.

Prolapse reduction	**Preoperative leakage with reduction**	
	N	**%**
All methods combined	112/584	19%
Pessary	5/88	6%
Manual	19/122	16%
Swab	32/158	20%
Forceps	21/98	21%
Speculum	35/118	30%

3.4.4 Clinical relevance of urodynamic investigation

Preoperative urodynamic testing with prolapse reduction in patients with advanced POP is sometimes used to diagnose occult stress incontinence and in an attempt to predict which patient are likely to benefit from an incontinence procedure at the time of prolapse repair. (48, 55, 59-61) In about 25-30% of the patients, the presence of SUI is not confirmed by urodynamic investigation. (62) Urodynamic investigation may be bothersome for the patient and up to 63% of the patients report dysuria after the examination and up to 20% have urinary tract infections. (63, 64) One study found that urodynamic testing before prolapse surgery was not cost-effective. (65) Because the predictive ability of preoperative urodynamic testing in patients with advanced prolapse is poor the diagnostic value is limited and remains an area of debate.

3.5 POP-Q

The pelvic organ prolapse quantification system (POP-Q) was introduced 1996 by the International Continence Society (ICS) for description of POP. (66) The POP-Q exam is used to quantify, describe, and stage pelvic support. There are six points measured at the vagina with respect to the hymen and additional three points, the total vaginal

length, genital hiatus and the perineal body in centimeters. Points above the hymen are negative numbers; points below the hymen are positive numbers (Table 2). The POP-Q system has underwent extensive testing and has been shown to have exceptional intra- and inter-examiner reliability in four studies involving 240 subjects. (67)

Table 2. Five stages of pelvic organ support as defined by the pelvic organ prolapse quantitation system.

Stage	Definition
0	No prolapse
I	The most distal portion of the prolapse is >1 cm above the level of the hymen
II	The most distal portion of the prolapse is ≤1 cm proximal or distal to the hymen
III	The most distal portion of the prolapse is >1 cm below the hymen but protrudes no further than 2 cm less than the total vaginal length
IV	Complete eversion of the total length of the vagina The distal portion protrudes at least the total vaginal length minus 2 cm beyond the hymen

3.6 Recurrence and defining success

The high rate of anatomical recurrence following traditional prolapse surgery is well known and especially the unsatisfactory recurrence rates after anterior vaginal wall repair. (18) (5, 68) About 30% of all surgery for prolapse and urinary incontinence is a secondary procedure due to recurrence. (15) (69) Anterior colporraphy is still the gold standard technique for anterior vaginal prolapse repair by central plication of the pubocervical fascia. In randomized trials the anatomical success rate of this procedure ranges from 40-60%. (4, 5) The failure rate in prolapse surgery depends on which definition of failure you use and whether failure is defined as subjective or objective failure. The definition of surgical success after prolapse repair is not standardized and the results vary greatly between studies. (70) In a study by Barber et al, 18 different surgical success definitions were evaluated in participants who underwent abdominal sacrocolpopexy. Treatment success ranged between 19.2% and 97.2% depending on which definition was used. The absence of vaginal bulge symptoms after surgery showed a significant association with patient's assessment of overall improvement, whereas anatomic success alone did not. (38)

A randomized trial that compared 3 different surgical techniques of anterior vaginal prolapse was conducted by Weber et al (5). The study found that at 23 months follow-up, POP-Q stage 2 prolapse recurrences was present in 70% patients after traditional anterior colporraphy, 54% after "ultralateral" anterior colporraphy, and 58% after absorbable mesh-augmented colporraphy. No statistically significant differences were found between the groups. The definition of *success* that was used in the trial was based on recommendations of 2001 National Institutes of Health (NIH). A secondary analysis of the trial of the 114 patients was performed at 2011 and then *success* was defined as 1) no prolapse beyond the hymen, 2) absence of prolapse symptoms, and 3)

absence of retreatment. Eighty-eight percent of the women met this definition of *success* at 1 year. (71)

3.7 Traditional surgical treatment of anterior POP

Surgical treatment for POP can be performed either by an abdominal or vaginal route but the vaginal route is preferred for most procedures. (72) There are many different combinations of defects in women with prolapse and combinations of surgery for anterior, apical or posterior vaginal wall prolapse are common. The aim of reconstructive surgery is to restore vaginal anatomy while maintaining normal bladder, bowel and sexual function. (73) There is a wide variety of surgical treatments but no consensus on which is the gold standard surgical procedure. Traditionally, anterior and posterior colporraphy are among the most frequently performed operations in prolapse surgery. (73)

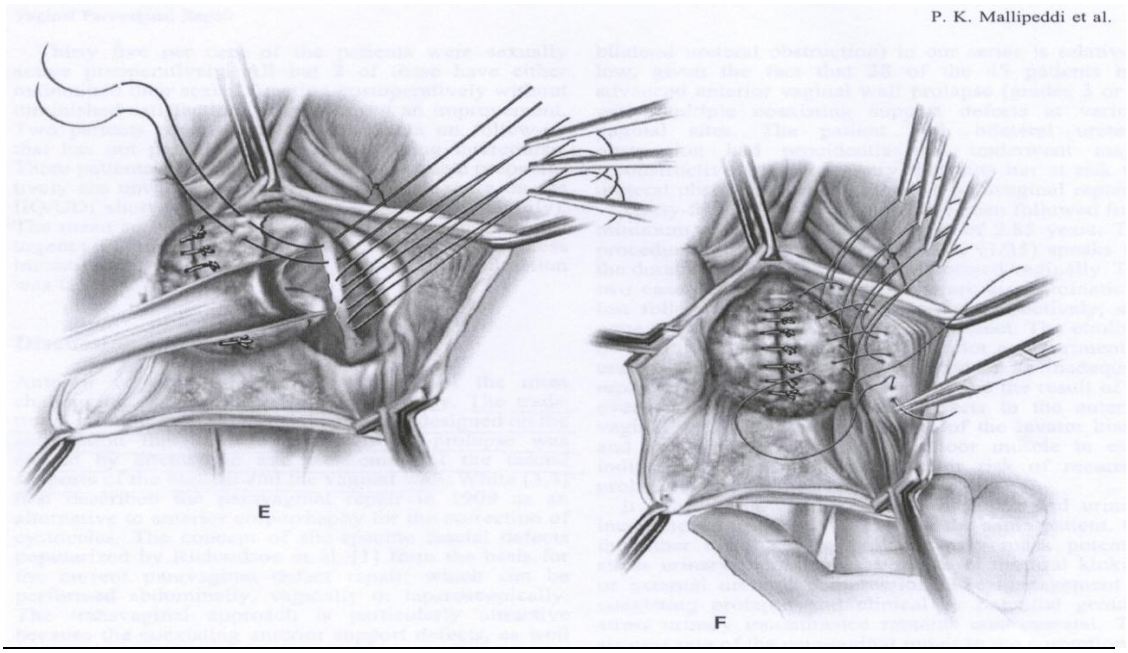
3.7.1 Anterior colporraphy

Anterior colporraphy was first described by Howard Kelly in 1914 and was originally an operation for stress urinary incontinence. (74) It was designed to improve urethra support by plication suture at the urethrovesical angle. The anterior vaginal wall is opened using a midline, sagital incision from the level of the cervix or vaginal cuff to a point 1.5 cm proximal to the external urethral meatus. The vaginal epithelium is dissected away from the underlying anterior pubocervical connective tissue using sharp dissection. The pubocervical tissue is then plicated in the midline using a series of interrupted or continuous delayed absorbable sutures. The anterior wall is closed with an absorbable suture. The success rate of this procedure ranges from 80–100% in cases series to 40–60% in randomized trials. (4, 5)

3.7.2 Paravaginal repair

The procedure is from the beginning identical to anterior colporraphy but the dissection extends more laterally to the ATFP where the pubocervical fascia is detached from the ATFP. The sharp dissection of the vagina from the bladder fascia continues laterally till the pelvic side wall can be identified. The obturator internus fascia and the ATFP are identified by palpation, and or visual inspection and a series of sutures are placed along the white line from the ischial spine to the symphysis (Figure 5 E+F). Paravaginal repair has a success rate between 67-100% for treatment of anterior vaginal prolapse, although the vaginal approach has a higher complication rate as compared to midline placation. (45, 75-78)

Figure 5. Vaginal repair in the correction of the anterior vaginal wall prolapse.



E) Paravaginal repair with sutures have been passed through the ATFP and through the pubocervical fascia.
F) Closing sutures through the pubocervical fascia and the vaginal wall.
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3.8 Mesh in vaginal prolapse surgery

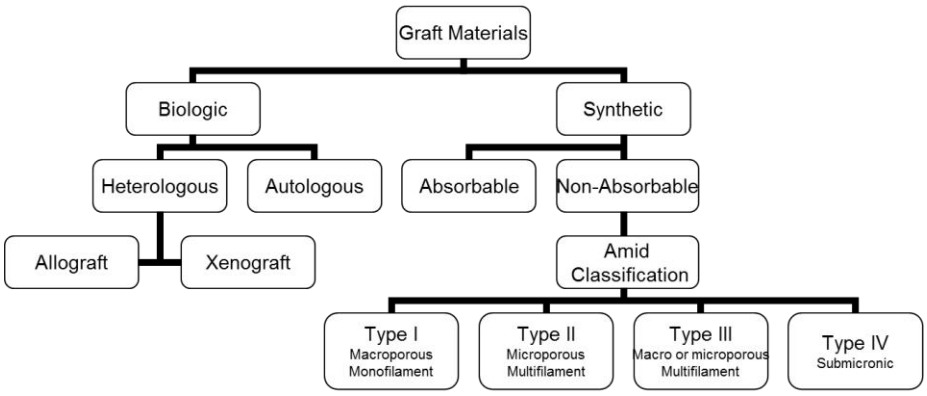
Graft materials have been used to replace and reinforce native tissue since the early 20th century. Prosthetic devices for abdominal hernia repairs have been found in ancient Egypt. (79) Grafts have been used for hernia repairs with a recurrence rate of 17% when used for incisional hernias, after an 81-month follow-up. (80) Permanent suture materials were first used in 1959 and in 1964 Ferguson was the first to introduce Marlex mesh. (81) In urogynecological surgery, many grafts have been used since then, mainly for incontinence surgery and vaginal vault suspensions. Since 1996, meshes have become increasingly popular for transvaginal surgical repair of POP. (82)

3.8.1 Graft materials

Biomaterials are defined as either biological or synthetic products used in surgery. Biological grafts can be further classified into autografts, allografts and xenografts. Autografts are harvested from the patient's own tissues. Allografts are taken from human donors (usually cadavers), whereas xenografts are taken from other species (e.g. porcine dermis or porcine small intestine). (83)
Synthetic grafts can be classified as absorbable (polyglactin 910 e.g. vicryl) and permanent grafts (i.e. polypropylene). Synthetic mesh has several advantages compared to biological grafts. They are readily available and do not require harvesting. Absorbable meshes encourage fibroblast activity and because of degradation (within 30-90 days) do not cause prolonged inflammatory reactions or infections. These benefits must be weighed against limited long term support.

Permanent meshes (non-absorbable) are classified into four subgroups (type I-IV) based on the weave and pore size (Figure 6). (84) Type I meshes are preferable over all other types of meshes because of less foreign body reaction, less risk for infection, rapid fibrinous fixation and greater tissue ingrowth compared to type II, III and IV meshes. (84, 85) Macroporous grafts have a pore size of more than 75µm (86) which allow migration and in-growth of fibroblasts, white blood cells and vascularized tissue. All mesh types induce a host-vs-graft reaction with foreign body giant cells and lymphocytes but the severity of the reaction differs between various materials. (87, 88) When used for the TVT procedure, macroporous, monofilament, polypropylene mesh has shown beneficial characteristics as compared with other synthetic biomaterials. (60)
Type I: Monofilament, macroporous knit which allows adequate in-growth of tissues and white blood cell response. Type I mesh have the lowest risk of erosions among the nonabsorbable synthetic grafts. (89) Examples Marlex, Prolene
Type II: Multifilament, microporous (<10 µm). Multifilament meshes cause more fibrosis. } E.g.GoreTex
Type III: Multifilament. Micro- or macroporous. E.g. Teflon, Mersilene, Dacron
Type IV: Submicronic, pore size (1 µm). Example Silicone, silicone-coated mesh. Rarely used in gynecological surgery.

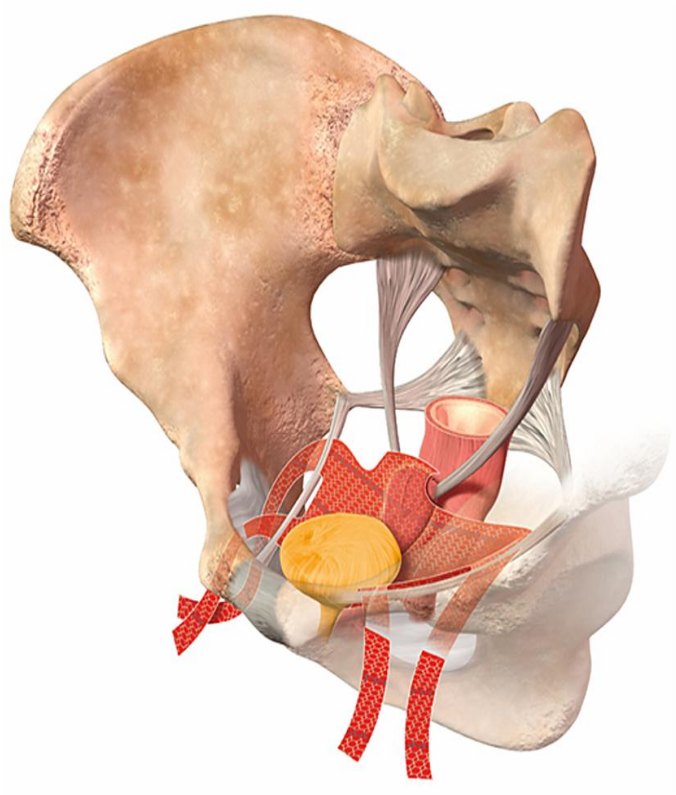
Figure 6. Classification of Biomaterials, Amid 1997



3.8.2 Mesh surgical procedure

The transvaginal mesh kit used in this thesis (Prolift®-system, Ethicon, Somerville, NJ) is a polypropylene type I mesh. The mesh is introduced using standardized metal trocars and mesh extension arms extends from the central part of the mesh to the ATFP (Figure 7). Four skin incisions are made in the anteromedial edge of the obturator foramen. The bladder is dissected to identify the ATFP and the arms are then passed through the ATFP and obturator foramen by the metal trocars. The central part of the mesh is positioned under the bladder after which the anterior vaginal wall is closed with an absorbable suture.

Figure 7. Anterior trocar guided transvaginal mesh.



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3.8.3 Management of anterior vaginal wall prolapse

Although data are limited, the Cochrane review from 2011 states that the polypropylene mesh anterior repair was superior to native tissue anterior colporraphy in reducing the risk of recurrent anterior compartment prolapse at objective anatomical evaluation. (53) Studies show high anatomical success rates ranging between 53-91%. No study was able to demonstrate a difference between the methods in terms of subjective success, quality of life outcomes, and reoperation rates for prolapse or incontinence. The dyspareunia rates were similar between the two procedures. Table 4 shows currently published studies on mesh surgery of the anterior vaginal wall with more than 12 months follow up. (90-97)

3.9 Complications of polypropylene mesh in prolapse surgery

In the literature the incidences and severity of complications varies greatly due to wide differences in surgical techniques, study design, methodology and follow-up time. Complications can broadly be classified into complications related to the surgical procedure and complications related to the mesh (Table 3).

Table 3. Perioperative complications

	Frequency:
Visceral injuries; bladder, rectum and urethra	2.4-4.4% (90, 98)
Haematoma requiring blood transfusion	1.4-2.5% (98)
Infections	2-3.8% (98)

3.9.1 Sexual function and dyspareunia

Dyspareunia is commonly reported in women with pelvic floor disorders.(99-101) A review of the effect of menopause on female sexual function found that by late menopause, 88% of women in the general population had sexual dysfunction with significant increases in dyspareunia. (99) The rate of de novo dyspareunia after traditional prolapse repair ranges between 14.5-36.1%. (101-104) Few studies address the problem of sexual dysfunction in women with POP after mesh surgery. The rate of de novo dyspareunia or worsened pain during sexual intercourse after trocar-guided mesh repair ranges between 2-44%. (93-95, 105, 106) Altman et al. reported deterioration in sexual function scores after mesh surgery, but not increased dyspareunia. (107) However in the RCT of Altman et al 7.3% in the mesh group reported pain during sexual intercourse which occurred "usually" or "always" compare to 2% in the colporraphy group (p=0.07). (90)

3.9.2 Urinary incontinence

De novo stress incontinence rate after trocar-guided mesh repair range from 7-24%. (90, 97, 105, 108, 109) In a retrospective study of 277 patients who did not have urinary incontinence before Prolift mesh repair, 23 patients (8.3%) underwent a suburethral sling insertion.(110)

3.9.3 Exposures

Mesh exposures are of major concern in mesh surgery. Exposures can occur at any time after surgery but are usually seen within the first year, (111) when the vaginal mucosa covering the mesh becomes thinned eventually exposing the mesh. This may result in vaginal discharge, bleeding, pain and discomfort. Exposures usually arise in the vaginal walls but can also be seen in the bladder or rectum and are visualized on vaginal examination, cystoscopy or rectosigmoidoscopy. Suggested risk factors are concomitant hysterectomy, smoking, increased BMI and age, as well as, an inverted T-incision or proximity to the vaginal scar. (111-114) Minor exposures often heal after local antibiotic or estrogen treatment, whereas larger exposures may need partial or total mesh excision and in rare cases extensive repeated surgery.

Table 4. Review of outcomes in the literature from 2008-2011 on the use of transvaginal mesh for pelvic organ prolapse

Author	Design	Method	Number of patients	Follow-up	Anatomical success (stage 0-1)	Exposures	De novo dyspareunia	De novo SUI
Altman 2011 (A)	RCT	Mesh (Prolift®)	200	1 year	82.3%	11.5%	7.3%	12.3%
		Traditional repair			47.5%		2%	6.3%
Withagen 2011 (A+P)	RCT	Mesh (Prolift®)	58	1 year	90.4%	16.9%	8%	12%*
		Traditional repair	56		54.8%		10%	11%
Sivaslioglu (2008) (A)	RCT	Mesh (Parietene®)	45	1 year	91%	6.9%	4.6%	0%
		Traditional repair	45		72%			7%
Cosson 2010 (A+P)	Prospective cohort	Mesh (Gynemesh®)	90	3 years	80.0%	14.4%	8.8%	NR
Moore 2010 (A)	Prospective cohort	Mesh (Perigee®)	114	2 year	88.5%	10.5%	6.4%	NR
Nieminen 2010 (A)	RCT	Mesh (Parietene®)	105	3 years	87%	19%	4%*	7%
		Traditional repair	97		59%		8%	5%
Elmer 2009 (A)	Prospective cohort	Mesh (Prolift®)	121	1 year	79%	11%		17%
Carey 2009 (A+P)	RCT	Mesh (Gynemesh®)	69	1 year	81%*	5.6%	27.8%	NR
		Traditional repair	70		65.6%		41.7%	NR
Nguyen 2008 (A)	RCT	Mesh (Perigee®)	38	1 year	87%	5.4%	8.7%	NR
		Traditional repair			55%		15.4%	NR

A= Anterior repair, P= Posterior repair. NR= not reported. * Not statistically significant ($p \geq 0.05$).

4 AIMS

The overarching aim of this thesis was to study the clinical outcomes of trocar guided transvaginal mesh surgery in women with anterior vaginal wall prolapse. The specific aims were:

1. To investigate the urodynamic effects of anterior vaginal wall prolapse surgery using either trocar guided transvaginal mesh or colporraphy. (Paper I)

2. To assess the effects of trocar guided transvaginal mesh on lower urinary tract symptoms after anterior vaginal wall prolapse repair. (Paper II)

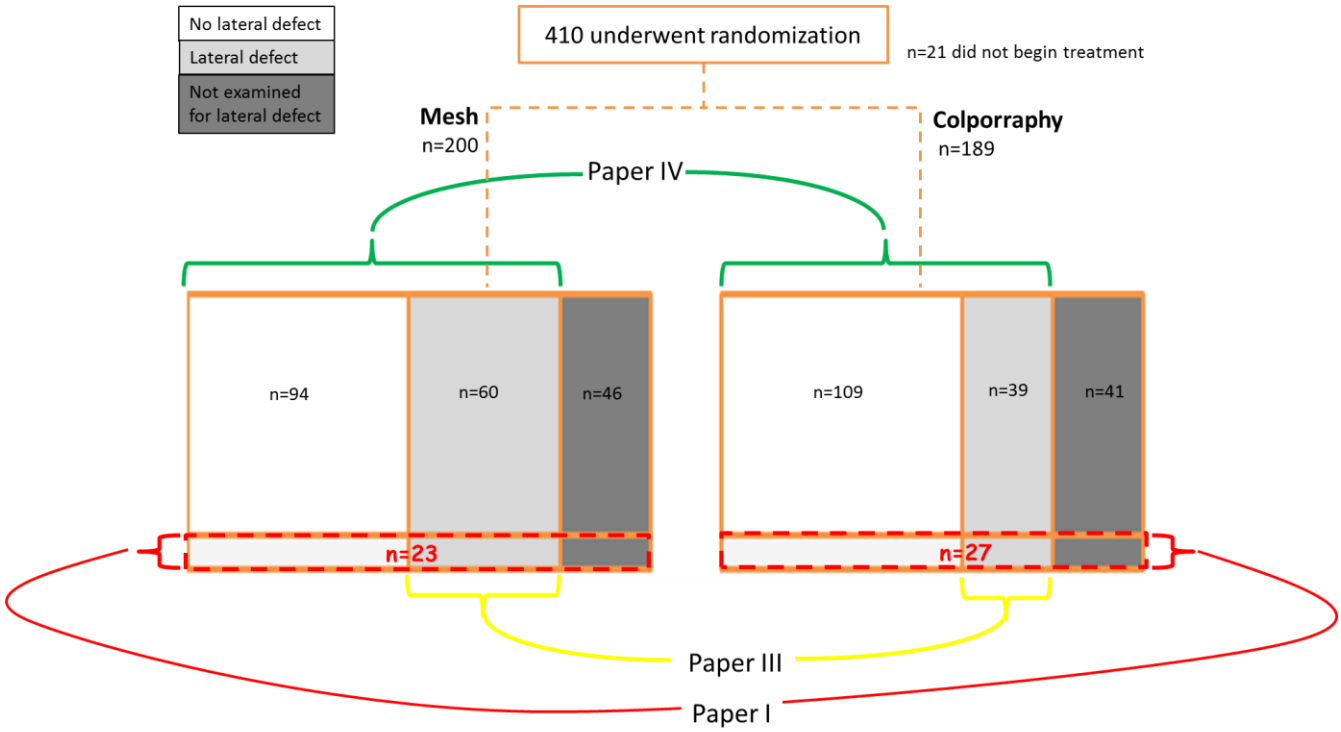
3. To evaluate objective and subjective outcomes following use of transvaginal mesh compared with traditional colporraphy for repair of anterior vaginal wall lateral defects. (Paper III)

4. To compare clinical characteristics and symptoms among patients with isolated central defects and patients with a combination of both central and lateral defects. (Paper IV)

5 PATIENTS

Paper I, III and IV are ancillary studies to a multicenter, randomized, controlled trial comparing the use of trocar-guided, transvaginal polypropylene-mesh repair kit and traditional colporraphy in women with prolapse of the anterior wall. (90) The study was performed at 53 hospitals in Sweden, Norway, Finland and Denmark from December 2007 through December 2008. In all, 1,685 patients were screened for enrollment of which 389 women were randomly assigned to treatment: 200 patients underwent transvaginal mesh kit repair and 189 patients underwent traditional colporraphy. The study included patients at least 18 years of age who presented with symptomatic primary or recurrent prolapse of the anterior vaginal wall ≥ 2 POP-Q stage. Exclusion criteria included previous cancer of any pelvic organ, systemic glucocorticoid treatment, insulin-treated diabetes, an inability to participate in study follow-up or to provide informed consent, or the need for concomitant surgery. The primary outcome was a composite of objective POP-Q stage 0-1 and the subjective absence of symptoms of vaginal bulging.

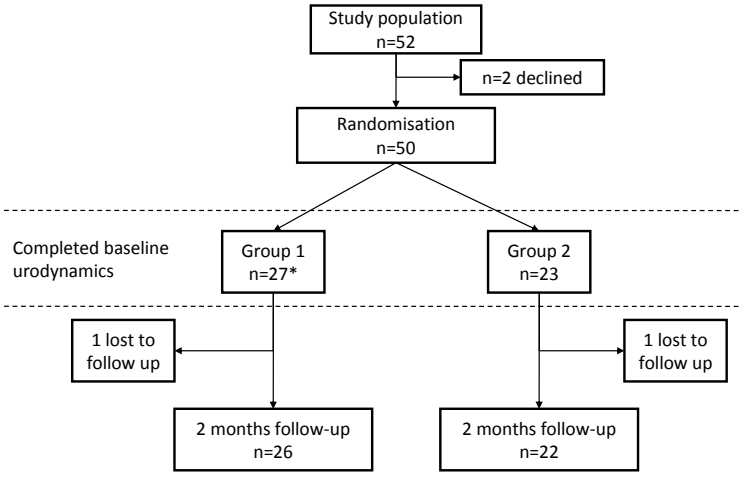
Figure 8. Disposition of patients in paper I, III-IV.



5.1 Paper I

The study population was enrolled at five hospitals in Sweden (Södersjukhuset, Danderyd hospital, University hospital at Huddinge and University hospital at Akademiska in Uppsala) and Denmark (Roskilde university hospital) and was a substudy to the larger RCT (see Figure 9). 50 patients underwent randomization: 27 patients underwent anterior colporraphy and 23 patient's trocar-guided transvaginal mesh. Mean age at the time of surgery was 66.3 (SD±10.8) years in the colporraphy group and 67.9 (SD± 11.3) years in the mesh group.

Figure 9. Randomization and follow-up of the study patients.



* One patient excluded from analyses because a prolapse pessary was not removed at the time of urodynamic assessment.

5.2 Paper II

Paper II is an ancillary study to a prospective multicenter cohort study performed throughout 26 clinics in Sweden, Denmark, Finland, and Norway from June 2006 through March 2007. Patients with symptomatic pelvic organ prolapse stage 2 or more were invited and during the study period, a total of 261 patients were included (of which nine patients were excluded due to missing information). The 1-year follow-up visit was attended by 232 (89%) patients. Anterior repair with mesh was performed in 121 of 261 patients (48%). The study population in paper II was restricted to women undergoing anterior repair with mesh with anterior vaginal wall prolapse stage ≥2 according to POP-Q (n=121). Eight patients were excluded from analysis due to incontinence surgery prior to the study, three patients because of stress urinary incontinence surgery performed within 2 months of the operation, and one patient was excluded due to erroneous data. In all, 109 patients with a mean age of 66.0 years (SD ±8.4) were available for analysis and 99 (91%) attended the 1-year follow-up visit. Of the 109 patients, 64 (59%) underwent surgery as a secondary procedure because of prolapse recurrence.

5.3 Paper III and IV

Of the 389 patients randomized and treated in the main study, 302 (78%) were examined for lateral defects at baseline. Of these patients, 99/302 (33%) were classified as having a lateral defect and 203/302 (67%) were classified as having no lateral defect. Paper III and IV include the 99 patient's positive for lateral defects at the baseline clinical examination, 39 underwent anterior colporraphy and 60 anterior trocar guided transvaginal mesh. Of the 99 patients, 36 (36%) underwent surgery as a secondary procedure because of prolapse recurrence. Twenty five patients were not examined for lateral defects postoperatively and were excluded from the final analysis. These patients did not differ with regard to baseline characteristics. Mean age at the time of surgery was 64 (SD±9.4) years in the colporraphy group and 63.6 (SD±9.6) years in the mesh group.

In paper IV the study population was derived from the same population as the study group in paper III but the inclusion criteria's were modified. In paper III we only included patients classified as having a lateral defect (n=99) but in paper IV we also included patients classified as having no lateral defect (n= 203) as controls. The final study population consisted of 302 women examined for lateral defects at baseline. Mean age at the time of surgery was 64 (SD±10.1) years in patients classified as having no lateral defect and 63.8 (SD±9.5) years in patients classified as having a lateral defect.

6 METHODS

Study design

Ethical approval from Research Ethics Committee at Karolinska Institutet was obtained prior to initiation of all studies (ethical permit numbers 2007/783-31/3 paper I, III and IV, 2006/382-31 paper II.

6.1 Paper I

A prospective, randomized multicenter trial evaluating the urodynamic effects of anterior vaginal wall prolapse surgery using either trocar guided transvaginal mesh or colporraphy. Clinical examination, subjective symptom, and urodynamic assessments were performed before surgery and at two months postoperatively (section 6.5). Methods, definitions, and descriptions of the urodynamic investigation conformed to the standards recommended by the International Continence Society. Trial protocols were send to the clinical research unit at the Department of Obstetrics and Gynecology, Danderyd Hospital, Stockholm, Sweden, and only the principal investigators had access to the data. All gynecologists participating in the trial were experienced pelvic surgeons and had pretrial, supervised, hands-on training in operating room sessions. The transvaginal mesh company had no influence over study aim, design, analysis and interpretation of data.

6.2 Paper II

This was a multicenter, prospective cohort study to assess the effect of trocar guided transvaginal mesh on lower urinary tract symptoms after anterior vaginal wall prolapse repair. All participants underwent anterior transvaginal mesh surgery using the trocar guided Prolift®-mesh kit and completed the validated Urogenital Distress Inventory (UDI) (section 6.5.4) before surgery and after one year.

6.3 Paper III

This was a secondary analysis from a randomized controlled trial of mesh kit versus anterior colporraphy. This parallel cohort study with randomized treatment allocation included 99 subjects diagnosed with a lateral anterior vaginal defect at baseline. Thirty-nine underwent anterior colporraphy and sixty anterior trocar guided transvaginal mesh surgery. Clinical examination (section 6.5.1 and 6.5.2) and subjective symptom assessments (section 6.5.4) were performed before surgery and one year postoperatively**.**

6.4 Paper IV

This was a cross sectional study and pre-decided subanalysis of a multicenter, randomized, controlled trial performed at 53 hospitals throughout Sweden, Norway, Finland and Denmark. The study population consisted of 302 women examined for lateral defect at baseline. Clinical examination and subjective symptom assessments were performed before surgery.

6.5 Clinical examination

6.5.1 POP-Q

Before surgery all patients underwent a gynecological examination in the supine position using the POP-Q system. (66) Methods, definitions, and descriptions conformed to the standards recommended by the ICS. (66) In prolapse surgery there is no universally accepted definition of failure and the POP-Q system does not include a definition of optimal vaginal topography. For the purpose of the studies presented in this thesis, the hymen plane was considered the point of reference for failure. Thus, recurrence of prolapse after surgery was defined as point Ba at the hymen or beyond (Ba≥0) (i.e. surgical failure) and no recurrence was defined as point Ba positioned proximal to the hymen (Ba<0). Postoperative point Ba proximal to the hymen (Ba<0) was considered anatomical cure. POP-Q measurements and staging at pre- and postoperative examinations were recorded in a separate protocol.

6.5.2 Lateral defects

The measurements of lateral defects are not included in the POP-Q system and there is no validated developed test to assess lateral defects. In the present studies we examined for lateral defects with the patient placed in the supine position. A speculum was used to depress the posterior vaginal wall after which a ring forceps was placed vaginally toward each ischial spine in an attempt to reduce the prolapse. The patient were straining when performing the lateral defect characterization. If the prolapse was completely reduced on one or two sides when ring forceps were applied the patient was positive for a lateral defect. The data on lateral defects were recorded prospectively as part of the protocol.

6.5.3 Urodynamics

Methods and guidelines from International Continence Society (ICS) were used for urodynamic measurement with uroflowmetry, filling cystometry, and combined pressure-flow studies. (115, 116)

Uroflowmetry
Uroflowmetry measures the flow rate (Q) of the urinary stream as volume per unit time in milliliters per second, (ml/s) and is performed to demonstrate the result of the emptying phase of the micturition cycle. The patient was asked to void when she felt a "normal" desire to void. Normal voiding occurs when the bladder outlet relaxes (is passive) and the detrusor contracts (is active). The flow patterns are described as continuous or intermittent.

Filling Cystometry
Cystometry was performed at a filling rate of 50 ml/minute to evaluate the storage phase of the micturition cycle and provided information on the capacity of the bladder (Maximum Cystometric Capacity) and the transmission of sensation through the neurosensory pathways (first sensation, first desire, strong desire and urgency). Stress-

test was performed at every 100 ml infused and if urinary leakage was observed in the absence of detrusor contractions the patient was diagnosed with SUI.

Urethral pressure
Urethral pressure measurements were used to assess urethral closure and voiding function. Urethral pressure is defined as the fluid pressure needed to open a closed urethra. The urethral pressure profile was measured along the whole length of the urethra. The simultaneous recording of both urethral (pura) and intravesical pressure (pves) enables calculation of urethral closure pressure, i.e., pura minus pves. Before maximum urethral closure pressure (MUCP) was determined, the volume was reduced to approximately 300 ml. The MUCP was determined while withdrawing the profilometer at 1mm/sec. The cough provocation test consisted of repeat coughing in a seated position. After voiding was complete the patient was catheterized and PVR urine was recorded.

6.5.4 Urogenital Distress Inventory

We used the UDI to collect data on lower urinary tract function and symptoms in paper II, III and IV. (117) We used the full version of the UDI which consists of 19 questions covering 3 domains of lower urinary tract function: symptoms related to stress urinary incontinence, detrusor overactivity, and bladder outlet obstruction. Response alternatives are measured on an ordinal scale based on frequency of symptoms. Self-reported bother caused by specific symptoms are recorded on a four- point scale with response alternatives ranging from 0 = not at all, 1= slightly, 2= moderately to 3 = greatly. The UDI consists of three subscales (each ranging from 0 to 100, with a maximum summary score of 300): irritative symptoms (UDI-I), obstructive discomfort (UDI-O), and stress symptoms (UDI-S). Higher scores indicate greater dysfunction. Data on the reliability, validity and sensitivity to change of these measures demonstrate that they are psychometrically strong. (117)

7 STATISTICAL ANALYSES

7.1 Paper I

Baseline characteristics are presented using absolute and relative frequencies (categorical variables) with either means and standard deviations (SD) or medians with ranges as appropriate. Non-parametric data were analyzed by using Wilcoxon signed rank test for dependent, and Mann-Whitney U-test for paired independent, samples. Fischer's exact or X^2 test was used for comparisons between proportions. All analyses were performed blinded to treatment allocation. Analyses were by intention to treat. One patient randomized to colporraphy underwent an anterior trocar-guided mesh procedure due to a misunderstanding at the trial site and this patient was analyzed as originally randomly assigned. We performed a statistical power analysis prior to the trial assuming a 25% difference in the proportion of patients with postoperative MUCP < 40 mm H2O, with β=0.8 and α=0.05. A sample size of at least 20 patients in each treatment arm were then required. Data were analyzed using SPSS version 17 software (Chicago, IL) and P-values < 0.05 were considered statistically significant for all comparisons.

7.2 Paper II

Analyses were restricted to patients responding to the questionnaires. Non-parametric continuous data were analyzed using the Mann-Whitney U-test for independent samples and Wilcoxon signed rank test for within group comparison. Fischers exact or $\chi 2$ test was used for comparisons between proportions when appropriate. Data were analyzed using SPSS® version 17 software (Chicago, Ill., US) and p-values < 0.05 were considered statistically significant for all comparisons.

7.3 Paper III

Baseline characteristics are presented using absolute and relative frequencies (categorical variables) with either means and standard deviations (SD) or medians with ranges as appropriate. The differences in UDI summary scores between groups were tested using the Mann-Whitney U-test. Comparisons of proportions of patients with lateral defects pre- and postoperatively were tested with Fischers exact test and presented as risk ratio with the 95% confidence intervals (CIs). Data were analyzed using SPSS® version 18 software (Chicago, Ill., US) and p-values < 0.05 were considered statistically significant for all comparisons.

7.4 Paper IV

Potential risk factors were assessed in uni- and multivariable models to determine the association with lateral defects: age, parity, body mass index (BMI), smoking, hormone replacement therapy (HRT), POP-Q staging of the anterior vaginal wall, previous anterior wall repair, previous posterior wall repair and previous hysterectomy. The continuous variables age and BMI were included partly as linear continuous variables (linearity was assessed by means of the partial residuals), and partly categorized using restricted cubic splines with 4 degrees of freedom. The Hosmer-Lemeshaw godness-

of-fit test was performed for the multivariable models and outliers were checked by means of the df-betas whereas the variance inflation factor (VIF) was used to detect possible multicollinearity. Interactions were tested for within the multivariable model. Data were analyzed using SPSS® version 18 software (Chicago, Ill., US) and R v2.9.2 (R.Foundation for Statistical Computing, Vienna, Austria) and p-values < 0.05 were considered statistically significant for all comparisons. Mann-Whitney U-test was used for comparing UDI-scores between groups.

8 RESULTS

8.1 Paper I

8.1.1 Patient characteristics

Fifty patients underwent randomization and underwent standardized urodynamics preoperatively and at two months after surgery. One patient randomized to colporraphy underwent an anterior trocar guided mesh procedure due to a misunderstanding at the trial site and because we applied intention to treat analyses this patient was analyzed as she was randomized. 27 patients were randomized to colporraphy, one patient was excluded from analyses because a prolapse pessary was not removed at the time of urodynamic assessment, and one patient did not want to undergo postoperative urodynamics. In total 25 (92.6%) patients in the colporraphy group were available for final analysis. In the mesh group 23 patients were randomized and one patient declined urodynamic assessment at the two months follow-up bringing a total of 22 (95.6%) patients available for final analysis. Age, BMI, number of overall parity, previous hysterectomy, and prolapse and incontinence surgery did not show any significant difference between the colporraphy and the transvaginal mesh group at baseline. Detailed descriptive data and statistical comparisons are presented in Table 5.

Table 5. Baseline characteristics

	Colporraphy (n= 27)	**Transvaginal mesh (n= 23)**	**p-value**
Age (mean±SD)	66.3±10.8	67.9±11.3	0.76
BMI (mean±SD)	24.7±3.2	25.7±3.5	0.28
Parity, median (range)	2 (1-5)	2 (0-4)	0.89
Previous surgery number of patients (%)	8 (30)	8 (35)	0.97
Prolapse surgery	2 (7)	4 (17)	0.39
Incontinence surgery	1 (4)	1 (4)	1.0
Hysterectomy	5 (18)	3 (13)	1.0

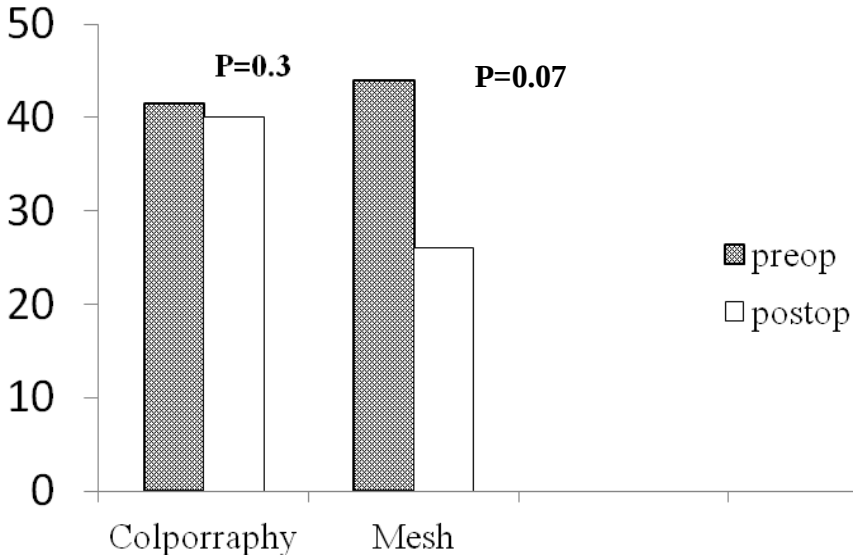
SD, standard deviation; BMI, body mass index.
Comparison between the two group's characteristics at baseline using Mann-Whitney or Fischer's exact or X^2 test was used for comparisons between proportions.

8.1.2 Urodynamic results

Table 6 shows the urodynamic findings before and after surgery in the colporraphy and the transvaginal mesh group. In the colporraphy group there were no significant differences in any of the urodynamic variables when comparing pre- with postoperative measures. After both anterior colporraphy and anterior trocar-guided transvaginal mesh there was an overall decrease in MUCP, although not statistically significant (p=0.3 and 0.07, respectively) (Figure 10). Foremost there was a shift in the

distribution of MUCPs quartiles toward a lower range of values (p= 0.008). After transvaginal mesh surgery the number of patients with MUCP< 40 cm H_2O increased although not at a significant level (p=0.18) but the number of patients with objective leakage at postoperative cough provocation increased significantly (p=0.016).

Figure 10. MUCP median preoperatively and at 2 months follow-up



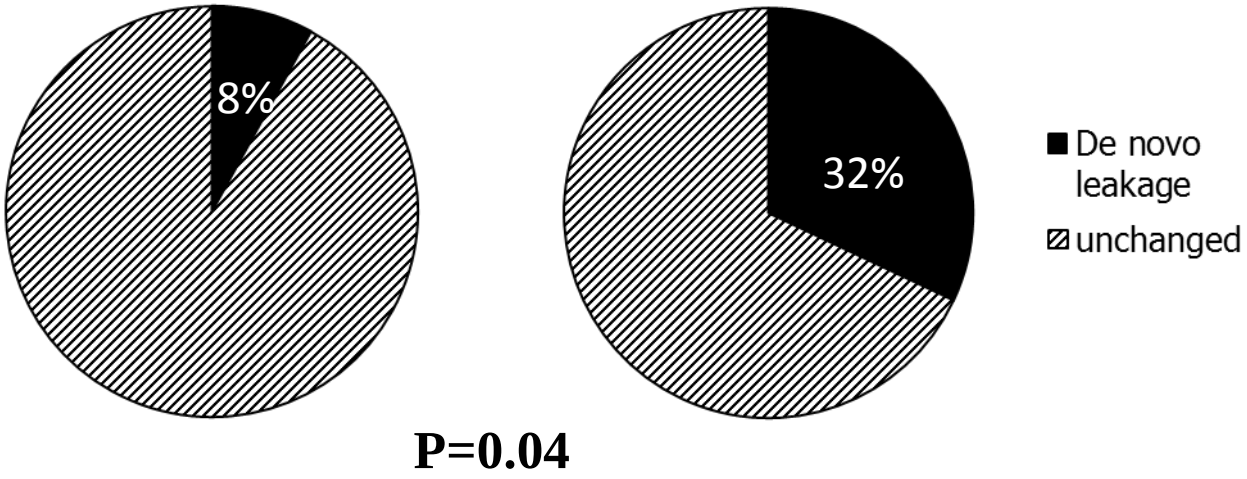
There was no significant differences in-between the groups with regard to postvoidal residual urine (PVR), maximal urine flow (Q-max), maximal cystometric capacity (MCC), sensation, detrusor contraction or MUCP postoperatively. There were, however, a significantly increased number of patients with de novo leakage at cough provocation after transvaginal mesh surgery when compared to colporraphy: de novo leakage at cough provocation was observed in 2/25 (8%) women after colporraphy and 7/22 (32%) women after transvaginal mesh (p=0.038) (Figure 11). Among the nine women with de novo leakage at cough provocation: six had a MUCP< 40 cm H2O; six had a BMI>25; and all patients were 65 years or older.

Table 6. Comparison Between Pre- and Postoperative Urodynamics

	Colporraphy			**Transvaginal mesh**		
	Preoperatively n=26	**Postoperatively n=25**	**p-value**	**Preoperatively n=23**	**Postoperatively n=22**	**p-value**
PVR (ml)	30.0 (0-150)	12.5 (0-200)	0.094	30.0 (0-150)	20.0 (0-200)	0.71
Q-max (ml/sec)	17.8 (7-48)	16.5 (5-36)	0.22	14.5 (3-33)	17.1 (6.6-48)	0.59
MCC (ml)	403 (253-573)	403 (176-562)	0.91	418 (191-811)	407(186-698)	0.18
First desire to void (ml)	243 (68-465)	242 (80-438)	0.69	248 (97-475)	226 (111-403)	0.56
Strong desire to void (ml)	354 (157-560)	345 (126-531)	0.98	390 (172-563)	354 (164-626)	0.70
Detrusor contraction during bladder filling (n affected/ n measured)	1/25	2/24	1.0	1/22	1/21	1.0
MUCP (cm H2O)	41.5 (23-98)	39.0 (5-100)	0.30	44 (6-69)	29.5 (14-79)	0.075
MUCP < 40 n (%)	12 (46)	13 (50)	1.0	9 (41)	13 (65)	0.18
MUCP < 28 1:st percentile	9 (34.6)	7 (26.9)		5 (22.7)	10 (50)	
MUCP < 43 2:nd percentile	15 (57.7)	16 (61.5)	}0.39	10 (45.5)	15 (75)	}0.008
MUCP < 53 3:rd percentile	21 (80.8)	20 (76.9)		16 (72.7)	16 (80.1)	
Leakage at cough (n affected/ n measured)	3/25	3/25	1.0	1/22	7/22	0.016

PVR, postvoidal residual urine; Qmax, maximal urine flow; MCC, maximal cystometric capacity; MUCP, maximal urethral closing pressure. Values are median (range) unless stated otherwise. Comparison between pre- and postoperative values using Wilcoxon signed rank test or χ^2 test.

Figure 11. De novo leakage at cough after Colporraphy and Transvaginal Mesh (%)



8.1.3 Stress urinary incontinence symptoms

Data from the stress subscale (UDI-S) of the UDI for the two groups showed that in the colporraphy group the UDI stress subscale improved from 33 (range 0-100) preoperatively to 8 (range 0-83) (p=0.06) at the two months follow-up. In the mesh group the UDI stress subscale did not change significantly from 16 preoperatively (range 0-100) to 17 two months postoperatively (range 0-100) (p=0.1). There were no significant differences between the two groups when comparing the distribution of UDI-S at two months follow-up, median 8 months (range 0-83) vs. 17 months (range 0-100) (p=0.09) in the colporraphy and mesh group respectively.

8.2 Paper II

8.2.1 Study group characteristics

109 patients were available for analysis and 99 (91%) attended the 1-year follow-up visit. UDI scores could be calculated for 96 patients preoperatively and for 94 patients postoperatively. Mean age± (SD) age at surgery was 66±8.4 years, mean BMI was 27.1±4.2 and median parity was 2 (range 0-5).
The majority of patients had undergone previous pelvic surgery and transvaginal mesh surgery was performed as a secondary procedure in a total of 64 (59%) patients.
Detailed cohort demographics are presented in Table 7.

Table 7. Patient characteristics

	Anterior repair (n=109)
Age (y)	66±8.4
Parity	2 (0-5)
Body mass index	27.1±4.2
Smoker	
Yes	9 (9)
No	99 (91)
Menopausal	
Yes	105 (96)
No	4 (4)
Hormone therapy	
Local	43 (40)
Systemic	29 (27)
Previous pelvic surgery	
Hysterectomy	50 (46)
Prolapse	64 (59)
Salpingo-oophorectomy	25 (23)
Concurrent surgery	20 (18)
Cervical amputation	1 (1)
Enterocele obliteration	1 (1)
Vaginal hysterectomy	3 (3)
Perineorraphy	5 (5)
Posterior colporraphy	8 (7)
Sacrospinous fixation	2 (2)

Figures are mean± standard deviation, median (range), or n (%).

8.2.2 Urogenital Distress Inventory (UDI)

Item-specific outcomes for the UDI with comparisons between pre- and postoperative scores are presented in Table 8. Postoperatively, there were significant decreases in all lower urinary tract symptom scores with the exception of leakage related to physical activity (P= 0.34), bedwetting (P= 0.09), and large and small amounts of urine leakage (P= 0.1 and 0.23, respectively). All items of the obstructive subscale improved significantly 1 year after surgery. Figure 12 is a box plot graph, illustrating the overall UDI preoperatively and at 1-year follow-up visit after surgery as medians with upper and lower quartiles. The overall UDI declined from 91 at baseline to 31 one year after surgery ($p<0.001$).

Figure 12. Box-plot graph of overall UDI at baseline and at the 1-year follow-up

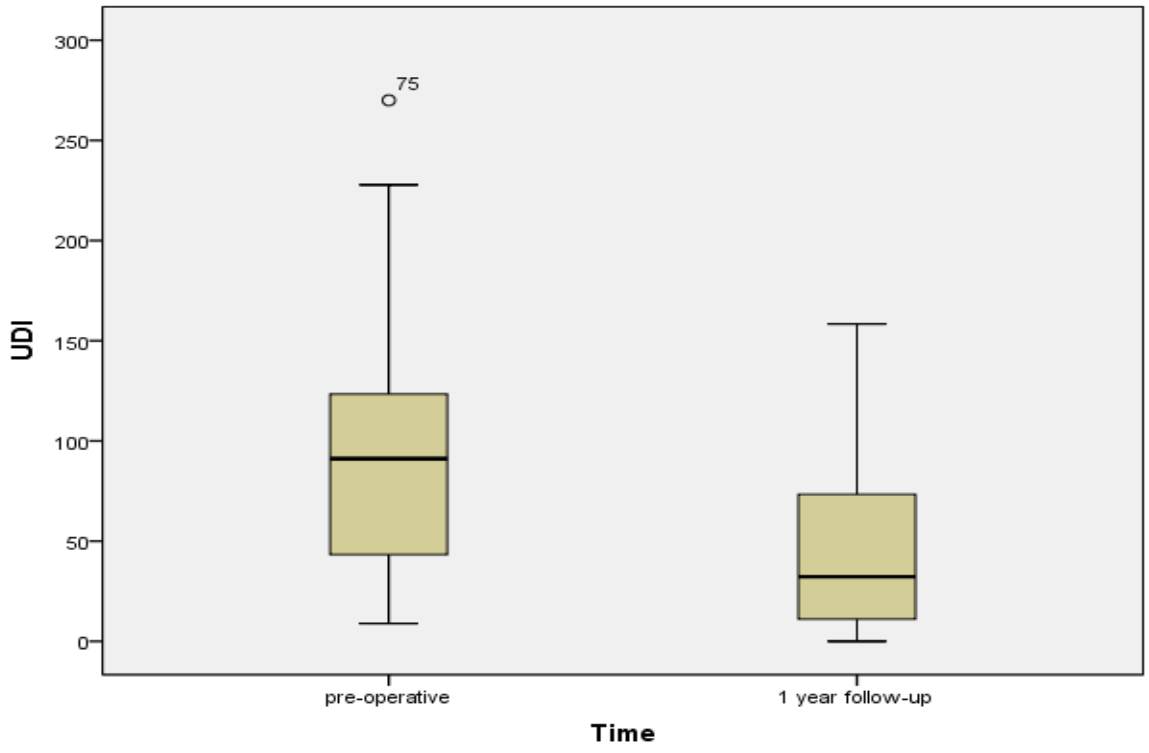


Table 8. Item specific outcomes according to the Urinary Distress Inventory

Do you experience, and, if so, how much are you bothered by:	Scale domain[1]	Preoperative score	1 year follow-up score	P-value
Frequent urination?	I	1.5±1.1	0.7±0.9	< 0.001
A strong feeling of urgency to empty your bladder?	I	1.5±1.2	0.6±0.8	< 0.001
Urine leakage related to the feeling of urgency?	I	1.1±1.1	0.5±0.7	< 0.001
Urine leakage related to physical activety, coughing or sneezing?	S	0.8±0.9	0.8±1.0	0.34
General urine leakage not related to urgency or activity?	O	0.5±0.8	0.3±0.5	0.003
Small amounts of urine leakage drops?	S	0.5±0.8	0.3±0.6	0.10
Large amounts of urine leakage?	I	0.5±1.0	0.4±0.7	0.23
Nighttime urination?	I	1.4±1.1	0.9±0.8	< 0.001
Bedwetting?	I	0.1±0.3	0.1±0.3	0.1
Difficulty emptying your bladder?	O	1.1±1.1	0.4±0.8	< 0.001
Feeling of incomplete bladder emptying?	O	1.2±1.07	0.4±0.7	< 0.001
Lower abdominal pressure?	O	1.2±1.2	0.3±0.6	< 0.001
Pain when urinating?	O	0.3±0.6	0.04±0.2	< 0.001
Pain in the lower abdomen or genital area?	O	0.4±0.9	0.1±0.3	< 0.001
Heaviness or dullness in the pelvic area?	O	1.4±1.1	0.3±0.6	< 0.001
A feeling of bulging or protrusion in the vaginal area?	O	2.1±1.1	0.3±0.8	< 0.001
Pelvic discomfort when standing or physically exerting yourself?	O	1.6±1.1	0.3±0.6	< 0.001
Push on the vaginal walls to have a bowel movement?	O	0.6±0.9	0.3±0.6	0.007

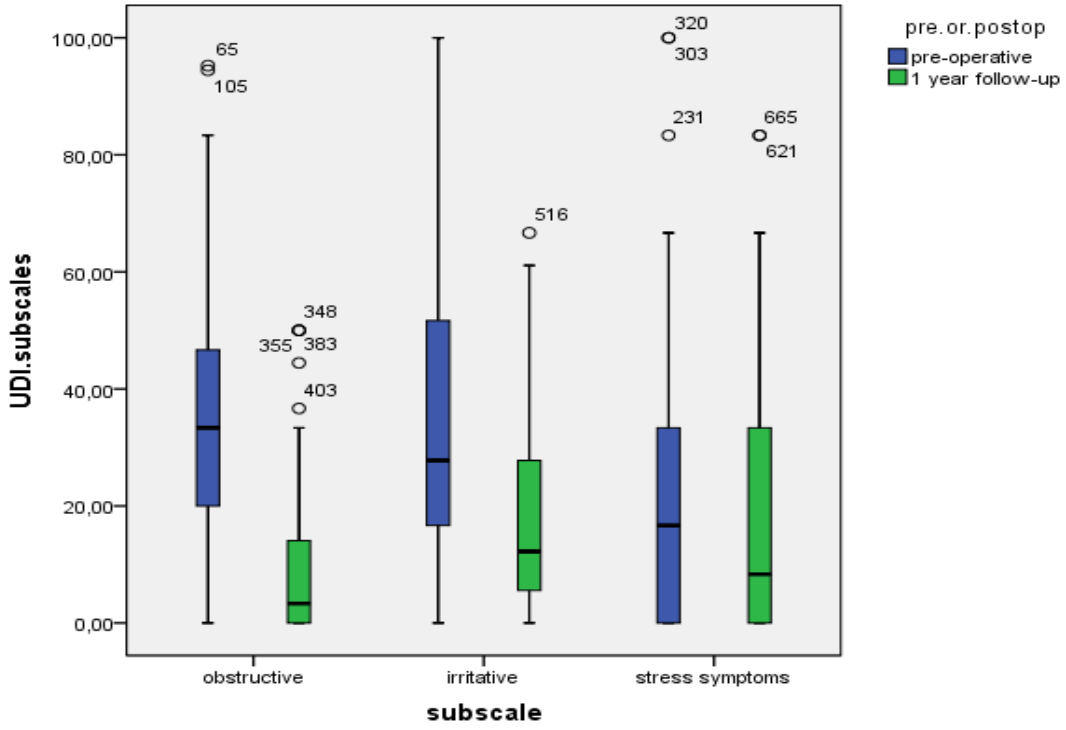
Data are mean± standard deviation.

[1]Subscale domains of the Urinary Distress Inventory: I= Irritative Symptoms; S= Stress Symptoms; O= Obstructive/Discomfort.

8.2.3 UDI subscales

Figure 13 shows box plot graphs of the three domains: symptoms related to bladder outlet obstruction (UDI-O), detrusor overactivity (UDI-I), and stress urinary incontinence (UDI-S), preoperatively and one year after surgery. In the irritative subscale the UDI decreased from 28 (range 0-100) to 11 (range 0-67) ($p<0.001$), the obstructive subscale from 33 (range 0-95) to 3 (range 0-50) ($p< 0.001$) and the stress subscale from 17 (range0-100) to 0 (range 0-83) ($p=0.11$).

Figure 13. Box plot graphs for comparison of the UDI subscales at baseline and at the 1-year follow-up



UDI in relation to anatomical outcome

Table 9 describes the UDI subscales preoperatively and at 1-year in relation to the anatomical outcomes after anterior transvaginal mesh surgery. Regardless of anatomical outcomes the irritative and obstructive subscales improved significantly one year after surgery with major improvements in average scores. For the stress subscale neither overall scores, nor the score in women with point Ba -1 cm or less proximal to the hymen, changed significantly one year after surgery.

Table 9. Comparison of outcomes in median with range of the Urinary Distress Inventory (UDI) and Subscales in relation to point Ba.

UDI	**Preop Overall (n=96)**	**1 year FU**	**p-value**	**Successful at 1 year follow-up (Point Ba-1cm or less) (n=72)**			**Failure at 1 year follow-up (Point Ba 0 or more) (n=22)**		
				Preop	1 year	p-value	Preop	1 year	p-value
UDI- I (0-100)	28 (0-100)	11 (0-67)	<0.001	28 (0-100)	13 (0-58)	<0.001	28 (0-100)	11 (0-47)	<0.001
UDI-O (0-100)	33 (0-95)	3 (0-50)	<0.001	33 (0-95)	3 (0-50)	<0.001	32 (3-94)	7 (0-50)	<0.001
UDI- S (0-100)	17 (0-100)	0 (0-83)	0.11	17 (0-100)	17 (0-83)	0.33	17 (0-67)	0 (0-50)	0.053
UDI score (0-300)	91 (9-270)	31 (0-58)	<0.001	93 (9-270)	36 (0-158)	<0.001	50 (20-200)	25 (0-127)	<0.001

Numbers are median scores (range). Comparisons are made for all patients (overall), for patients with beneficial anatomical results at the 1 year follow up (Ba-1 cm or less) (n=72) as well as for patients with anatomical failure at the 1 year follow up (Ba 0 or more) (n=22). FU=Follow-up. UDI I= irritative subscale, O= obstructive subscale, S= stress subscale

UDI in relation to primary or secondary procedures

Of the 109 patient, 64 (59%) underwent surgery as a secondary procedure because of prolapse recurrence. Tables 10 show the UDI subscales at baseline in relation/comparison to primary or recurrent prolapse status. For primary procedures all three subscales of the UDI improved at 1 year follow-up. For secondary procedures, the irritative and obstructive subscale improved whereas the stress scale was unchanged.

When comparing the two groups, patients who had undergone a primary procedure had a lower overall UDI-score than those who had a secondary operation (p=0.03). Between groups comparisons further showed that primary cases had lower scores in the stress scale (p=0.049), whereas for symptoms in the irritative domain, scores were lower after having secondary procedure (p=0.009) (Table 10).

Table 10. Comparison of lower urinary tract symptoms for: A) pre- and postoperative scores within groups, and B) pre- and postoperative scores between groups.

A	**Primary procedure (n=45)**			**Recurrency (n=64)**		
	Preoperatively	**1 year follow-up**	**P-value**	**Preoperatively**	**1 year follow-up**	**P-value**
UDI-I	36±28	29±15	<0.001	33±24	20±17	<0.001
UDI-O	36±22	8±11	<0.001	35±21	11±13.5	<0.001
UDI-S	22±27	13±20	0.02	22±21	23±24	0.856
Overall UDI score	91±64	35±37	<0.001	88±49	54±45	<0.001

	Preoperatively			**1 year follow-up**		
B	**Primary procedure**	**Recurrency**	**P-value**	**Primary procedure**	**Recurrency**	**P-value**
UDI-I	36±28	33±24	0.765	29±15	20±17	0.009
UDI-O	36±22	35±21	0.750	8±11	11±13.5	0.59
UDI-S	22±27	22±21	0.505	13±20	23±24	0.049
Overall UDI score	91±64	88±49	0.749	35±37	54±45	0.03

Figures are mean± standard deviation.
Subscale domains of the Urinary Distress Inventory: I= Irritative Symptoms; S= Stress Symptoms; O= Obstructive/Discomfort.

8.2.4 Stress urinary incontinence

Figure 14. Symptoms of stress urinary incontinence at baseline and one year after mesh surgery.

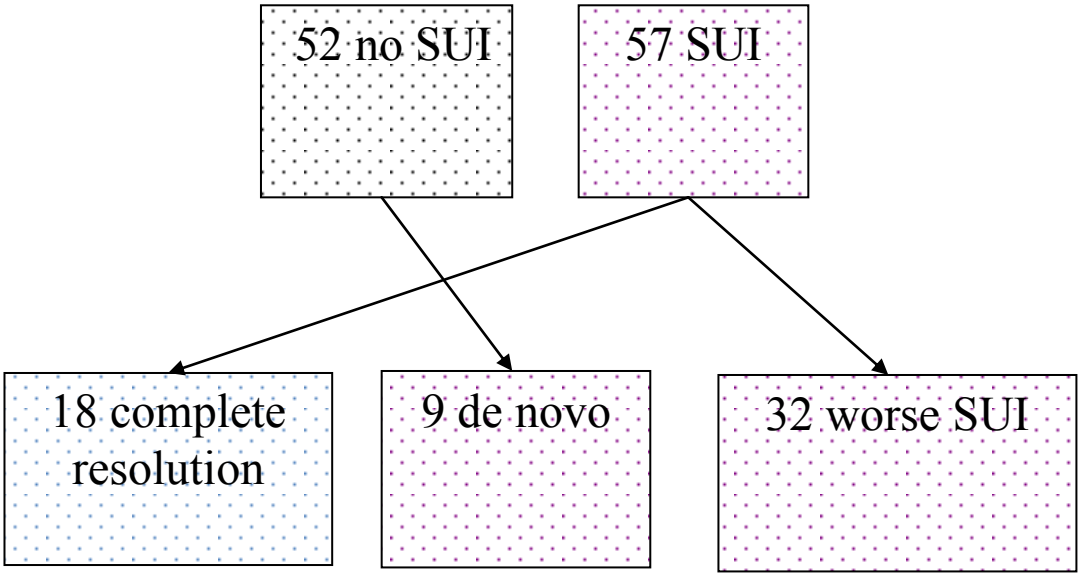


Figure 14 shows the change in stress urinary incontinence symptoms prior to surgery and at the one year follow-up. When we analyzed individual outcomes, the question "Urine leakage related to physical activity, coughing, or sneezing", at baseline, 57/109 patients (52%) reported any stress urinary incontinence. Postoperatively, 18/57 patients (32%) reported complete resolution of stress urinary incontinence symptoms whereas 32/57 patients (56%) reported aggravated stress incontinence. A further nine patients reported de novo stress urinary incontinence, which combined with three patients having stress urinary incontinence surgery brings the rate of de novo stress symptoms to 11%.

8.3 Paper III

Of the 389 patients randomized and treated in the large RCT study, 302 (78%) were examined for lateral defects at baseline. Of these patients, 99/302 (33%) were classified as having a lateral defect and 203/302 (67%) were classified as having no lateral defect.

8.3.1 Subject characteristics

The final study population available for analysis included 99 women having a lateral defect at baseline clinical examination. Detailed descriptive data and statistical comparisons are presented in Table 11. Women who underwent transvaginal mesh surgery had a higher BMI than in the colporraphy group, otherwise there were no other differences between the group regard to baseline characteristics.

Table 11. Characteristics of the study cohort.

Characteristic	**Colporraphy (n=39)**	**Transvaginal mesh (n=60)**	**p-value**
Age at surgery (years)	64 (±9.4)	63.6 (±9.6)	0.71
Body mass index (kg/m^2)	25.0 (±3.0)	26.4 (±2.9)	0.01
Number of childbirths†	2 (1-4)	2 (0-5)	0.20
Cesarean deliveries	1 (2.6)	0 (0.0)	0.40
Current smokers	2 (5.1)	11 (18.3)	0.06
Age at menopause (years)	49.5 (±4.8)	50.2 (±4.8)	0.35
Current use of hormone	29 (74.4)	36 (60.0)	0.14
Previous pelvic surgery	13 (35.1)	23 (38.3)	0.75
anterior repair	7 (18.9)	9 (15.0)	0.61
posterior repair	5 (13.5)	8 (13.3)	1.0
Hysterectomy	10 (27.0)	17 (28.3)	0.89
Incontinence surgery	4 (10.8)	5 (8.3)	0.73
UDI‡	91.5 ±52.4	89.6±47.5	0.93
POP-Q stage			
II	15 (38.5)	25 (41.7)	0.75
III	24 (61.5)	35 (58.3)	
Point Ba≥ 0	38 (97.4)	59 (98.3)	0.35

Figures are number of patients (%). Means ± SD.
†Median with range. ‡ Responses to the Urogenital Distress Inventory (UDI), questionnaires combine to form overall scores which are presented as mean±SD. Comparison using Mann-Whitney U-test. Fischer's exact or X^2 test was used for comparisons between proportions.

8.3.2 Anatomical outcomes

One year after surgery, a persistent lateral defect was significantly more common after colporraphy (11/32 patients, 34.4%) compared to transvaginal mesh (1/42 patients, 2.4%), (P<0.001) (Figure 15A). This corresponded to a risk ratio of 14.4 (95% CI 2.0-106.1). Patients who were not examined for lateral defects at baseline or postoperatively did not differ from those who were examined in any significant way regarding to clinical characteristics.

One year after surgery, having an anatomic recurrence as defined by the POP-Q was also significantly more common in the colporraphy group (16/38 patients, 41.7%) compared to the transvaginal mesh group (4/58 patients, 6.9%) (P<0.001) (Figure 15B). In the colporraphy group, patients with no lateral defects had significantly less anatomic POP-Q failures at one year compared to patients with lateral defects, 19% vs 73% (p= 0.006). In the mesh group the small number of patients with both anatomical recurrence, as well as, persistent lateral defects, did not allow for a statistical comparison.

Figure 15.
Comparison between groups at 1-year follow up

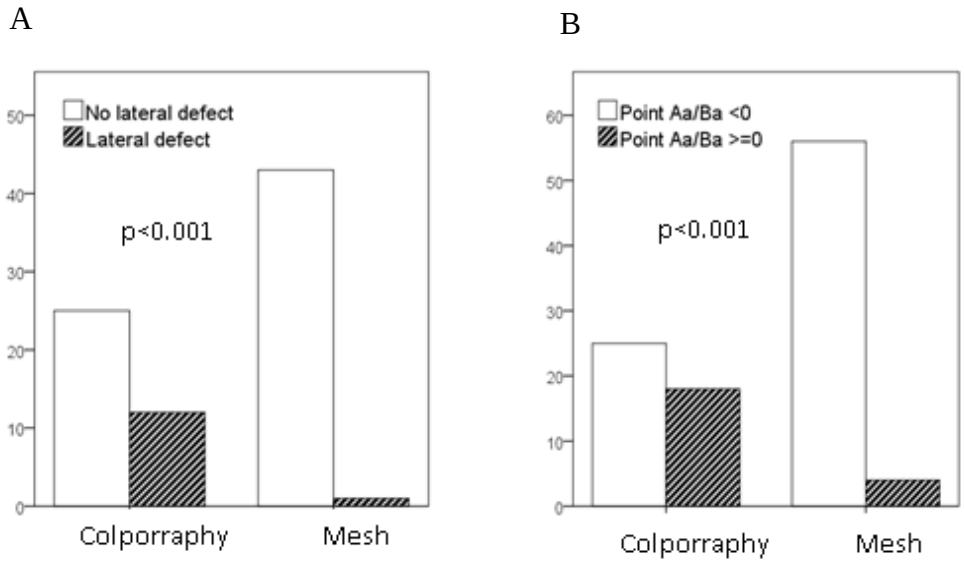


Figure A shows less lateral defects in the mesh group compared to the colporraphy group at the one year follow up.
Figure B shows better anatomical outcome in the mesh group compared to the colporraphy group at the one year follow up.
Figures are number of patients. Comparison using Fischers exact test.

8.3.3 Symptoms

This analysis included the women who had answered the UDI questionnaire at entry and at one year follow up (n=75.) Table 12 shows the UDI outcomes after colporraphy and transvaginal mesh. There were no significant differences between the groups with regard to subjective symptoms neither according to the overall UDI score, nor the UDI subscales at one year follow-up. However, patients in the colporraphy group with no lateral defects at follow up showed a significant improvement in the obstructive subscale (measuring the sensation of bulging and heaviness) compared to those with

persistent lateral defects (P= 0.03). In the mesh group only one patient had a persistent lateral defect one year after surgery, making comparisons impossible.

Table 12. Urogenital Distress Inventory (UDI) after Colporraphy and Transvaginal mesh

	Colporraphy Mean difference from baseline (n=32)	**Mesh Mean difference from baseline (n=43)**	**p-value**
Total UDI	37.3±50.6	39.0±45.8	0.61
UDI-I	12.1±19.9	11.2±18.5	0.91
UDI-S	4.3±28.2	1.5±24.1	0.65
UDI-O	20.4±16.1	22.9±19.5	0.33

UDI scores and UDI subscales changes from preoperative to one year follow up assessments, shown for both groups.
Comparison using Mann-Whitney U-test
Mean difference ± standard deviation

8.4 Paper IV

8.4.1 Subject characteristics

Patients characteristics for women having no lateral defects (n=203) and patients with lateral defects (n=99) are presented in Table 13.

Table 13. Subject demographics and clinical characteristics (n = 302)

Demographics	**No lateral defect (n=203)**		**Lateral defects (n=99)**	
	n	**%**	**n**	**%**
Age at surgery				
≤ 50	14	6.9	4	4
51-70	132	65.0	70	70.7
≥ 71	57	28.1	25	25.3
Parity				
≤ 1	22	11	14	14.3
≥ 2	178	89	84	85.7
Body mass index (kg/m^2)				
< 25	83	46.6	32	36.4
25-30	73	41.0	47	53.4
> 30	22	12.4	9	10.2
Smokers	29	14.5	13	13
Postmenopausal	182	89.8	92	93
Hormone replacement therapy at baseline				
peroral	21	10.3	25	25.3
local	83	40.9	40	40.4
non	99	48.8	34	34.3
Previous anterior vaginal wall repair	46	22.9	17	17.2
Previous hysterectomy	45	22.3	30	30.3
Previous posterior vaginal wall repair	22	10.8	13	13.1
POP-Q				
stage II	85	42	40	40
stage III	118	58	59	60

Data are n (%)

8.4.2 Uni- and multivariable logistic regression model

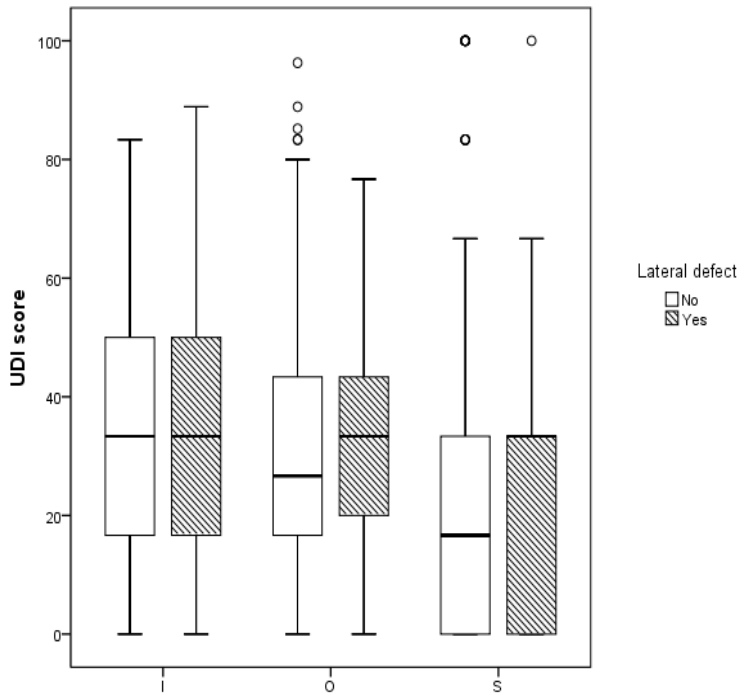
The uni- and multivariable analysis of clinical covariates associated with lateral defects included 174 patients with no lateral defect and 87 with lateral defects. A number of factors were assessed in uni- and multivariable models to determine the association with lateral defects: age, parity, BMI, smoking, hormone replacement therapy (HRT),

POP-Q staging of the anterior vaginal wall, previous anterior wall repair, previous posterior wall repair and previous hysterectomy. In the univariable analysis only oral HRT variable turned out to be significantly associated with lateral defects OR 3.5 (95% CI 1.7-7.0) ($p<0.01$). In the final multivariable analysis all the variables included in the univariable analysis were considered. Oral use of HRT and previous anterior vaginal wall repair turned out to be significantly associated with lateral defects (OR 2.7, 95% CI 1.2-6.3 and OR 0.3, 95% CI 0.1-0.9 respectively). Previous anterior vaginal wall surgery decreased the odds for having a lateral defect in the multivariable analysis. Age and BMI were also included as continuous variables in the multivariable model and modeled partly as linear predictors and partly using restricted cubic splines as a sensitivity analysis in case the categorisation of these variables was non optimal. Neither variable showed any association with lateral defects in the models ($p= 0.29$; 0.72 (linear model) and $p= 0.05$; 0.49 (spline model) for age and BMI respectively). The p-value from the Hosmer-Lemeshaw godness-of-fit test was 0.865 and the fit of the model can therefore be considered as acceptable. No outliers were detected and the largest VIF value was 2.4 (for age), so multicollinearity was deemed low. There were no statistically significant interactions between any of the variables.

8.4.3 Urinary Distress Inventory score

There were no statistically significant differences between the two groups in any of the three UDI subscales (irritative, obstructive or stress) ($p=0.78$, $p=0.60$, $p=0.77$) (Figure 16). Only one question in the questionnaire showed a significant difference; "A feeling of bulging or protrusion in the vaginal area" was higher scored in the group with combined midline and lateral paravaginal defects ($p=0.02$).

Figure 16. The three subscales of the Urinary Distress Inventory shown for patients with and without lateral defects.



I=Irritative, O= Obstructive, S= Stress, There were no differences between the two groups in any of the three subscales ($p=0.78$, $p=0.60$, $p=0.77$).

Table 14. Uni- and multivariable analysis of clinical covariates association with lateral defects.

	Univariable			Multivariable		
	Odds ratio	**95% CI**	**p-value**	**Odds ratio**	**95% CI**	**p-value**
Age (years)			0.50			0.72
≤ 50	0.7	0.2-2.2	0.49	0.6	0.1-4.4	0.59
51-70	1.2	0.7-2.1	0.70	1.2	0.6-2.2	0.69
≥ 71	Reference			Reference		
Parity ≤ 1	Reference			Reference		
≥ 2	0.7	0.4-1.5	0.41	0.6	0.3-1.4	0.25
BMI (kg/m^2)			0.16			0.42
< 25	Reference			Reference		
25-30	1.7	1.0-2.9	0.07	1.5	0.8-2.6	0.20
> 30	1.1	0.4-2.6	0.89	1.1	0.4-2.7	0.90
Smokers	0.9	0.4-1.8	0.75	0.9	0.4-1.9	0.70
Postmenopausal	1.5	0.6-3.7	0.36	1.3	0.3-5.4	0.75
Estrogen replacement therapy at baseline			<0.01			0.06
non	Reference			Reference		
local	1.4	0.8-2.4	0.22	1.2	0.7-2.3	0.52
peroral	3.5	1.7-7.0	<0.01	2.7	1.2-6.3	0.02
Previous anterior vaginal wall repair	0.7	0.4-1.3	0.25	0.3	0.1-0.9	0.02
Previous posterior vaginal wall repair	1.2	0.6-2.6	0.56	2.1	0.7-6.3	0.19
Previous hysterectomy	1.5	0.9-2.6	0.13	1.2	0.6-2.5	0.57
POP-Q stage II	Reference			Reference		
stage III	1.0	0.6-1.7	0.87	1.0	0.6-1.7	0.92

Adjusted for all variables in Table 13.

Analysis included 174 patients with no lateral defect and 87 with lateral defect.

Note: BMI, body mass index; CI, confidence interval.

9 DISCUSSION

9.1 Paper I

In this randomized urodynamic study we found that trocar-guided transvaginal mesh repair of anterior vaginal wall prolapse is associated with a significant increase in objective de novo stress urinary incontinence compared to anterior colporraphy. Stress urinary incontinence often co-exists with POP, particularly when the prolapse is mild. (40) In contrast, women with advanced prolapse are less likely to have SUI (39) which can explain the low frequency of leakage at cough in our study population at baseline 4/47 (8.5%) where 38% of the women had stage III prolapse. We used the ICS definition of urodynamic stress incontinence, with cough provocation during filling cystometry in the absence of detrusor contraction. De novo leakage at cough provocation was observed in 2/25 (8%) women after colporraphy and 7/22 (32%) women after transvaginal mesh (P= 0.038). Our findings corroborate a previous prospective clinical cohort study on the use of trocar-guided transvaginal mesh suggesting that even though most lower urinary tract symptoms decreased after surgery, stress urinary incontinence did not. (92) In a published retrospective study of sixty patients who underwent total vaginal mesh repair without midurethral sling after negative preoperative urodynamics, fifteen (25%) patients were diagnosed with de novo stress urinary incontinence. (118) These findings are consistent with another retrospective study of 309 patients by Aungst et al. (109) in which the rate of de novo stress incontinence after transvaginal mesh repair was 24.3%.

The cause of de novo SUI after prolapse correction is not fully understood. It is thought that correcting the prolapse eliminates the dynamic obstruction of the urethra and therefore allows for stress related urine leakage. It is possible that the effective suspension of the anterior vaginal wall and bladder neck during trocar-guided transvaginal mesh surgery affects urethral support and urethral closure to a greater extent than colporraphy i.e. over-corrects the urethra and bladder neck. The mesh may also deflect the urethrovesical junction posteriorly as a result of excessive tensioning or contraction of the mesh postoperatively. It could also be explained by mesh techniques causing greater and wider perioperative dissection causing instability to the suburethral layer or injury to the urthral innervation. The effectiveness of the urethral compression mechanism is dependant of the layer formed by the connection of the endopelvic fascia and anterior vaginal wall to the arcus tendineus fascia pelvis (46) and the mesh may affect the stability of the suburethral layer and mobility of the urethra.

The MUCP, defined during urethral pressure profiling, represents the highest pressure along the functional length of the urethra. In our study, MUCP decreased in both groups after surgery but the decrease was more pronounced in the mesh group. In the mesh group, MUCP was lower postoperatively compared to baseline (44 to 26, p=0.07) and the distribution of MUCP (in quartiles) (p=0.008) tended to move to lower values. The MUCP has been reported to correlate with stress incontinence severity and with surgical outcomes in some studies, but not in others, and the reproducibility of urethral pressure profile parameters is poor. (119) Some studies have found no difference in average MUCP in women with and without SUI, whereas other studies have found that

urethral pressures are lower in women with SUI. (119) Thus the predictive value is doubtful and urethral pressure profiling cannot be used as a diagnostic test for SUI in a clinical setting.

In our study population, only two patients had detrusor contractions during bladder filling preoperatively. Some studies suggest that the sensitivity of clinical diagnosis is better than that obtained with urodynamic testing, because more than 50% of patients with subjective urge urinary incontinence have normal urodynamic studies and that detrusor overactivity may be observed on cystometry in about 10% of asymptomatic women. (120) We neither observed increased postvoidal residual urine volumes, nor decreased urine flow velocities, within the treatment groups before and after surgery, or when comparing the two groups postoperatively. Although this in agreement with previous reports based on self-reported outcomes, (92) a supposed change of the urethral and bladder neck angulation would be expected to give rise to adverse changes also in urodynamic variables associated with bladder emptying. On a similar note, we found no indications of reduced cystometric bladder capacity, decreased bladder sensitivity, or an increase in detrusor contractions during bladder filling.

Evidence of leakage during cough in the absence of a detrusor contraction was recorded as urodynamic evidence of SUI. Several studies have demonstrated that when stress incontinence is the only symptom, urodynamic stress incontinence is likely to be present in 90% of cases but the relationship between urge incontinence and detrusor overactivity is less evident. (121, 122) Though the positive predictive value of urodynamic testing for SUI the sensitivity is moderate at best. (121, 122)

9.2 Paper II

We found that anterior vaginal wall prolapse surgery using a trocar guided transvaginal mesh kit resulted in significant improvements of self-reported obstructive and irritative lower urinary tract symptoms. In concurrence with previous reports, transvaginal mesh repair of the anterior vaginal wall did not result in overall improvement of stress urinary incontinence. (90, 123-125) We used the ICS definition of symptoms of stress urinary incontinence, which is based on two validated questions in the UDI. (126) De novo stress urinary incontinence occurred in 12/109 (11%) and 32/57 (56%) reported worsening SUI. However at baseline only 52 of the 109 patients did not have any symptoms of SUI, whereas 57 patients did. Hence, of the patients at risk 23% (12/52) reported de novo SUI. Comparing our results with the Cochrane review of surgical management of prolapse, (53) our study population showed higher rates of de novo SUI (23% vs 15%) which could possibly be explained by the significant heterogeneity when the data from all the trials were combined in a meta-analysis.

Comparing six newly published randomised controlled trials on transvaginal mesh vs. traditional surgery for repair of the anterior vaginal wall, the frequency of de novo SUI after mesh repair ranged between 0-12%. (90, 91, 95-97, 127) However in two trials the frequency of concomitant mid-urethral sling was 49-70%. (91, 95) and in two trials the frequency of de novo SUI was not reported. (91, 95) In three out of six of the RCT: s, concomitant vaginal hysterectomy was performed in 30-60%. (91, 95, 96) These

differences make it difficult to compare the effect on SUI, which was a secondary outcome in all six studies.

Although overactive bladder symptoms should be considered an important adverse outcome after prolapse surgery but the occurrence of this symptom complex is rarely reported separately. The effect of urge urinary incontinence and prolapse surgery is limited and inconclusive. (53) In concordance with the literature we found an improvement of irritative symptoms such as frequent urination, urgency, nocturia and urge incontinence after trocar guided mesh surgery. (90, 125, 128) Resolution of symptoms in the irritative and the obstructive domains were present regardless of anatomical outcomes. Although the procedure improved irritative symptoms in both recurrent and primary prolapse cases ($p<0.001$), the relief of irritative symptoms were more pronounced in the group of patients having the procedure for recurrent prolapse ($p=0.009$). The reason for this observation is not clear and deserves further investigation.

In this study, 44% (25/57) of preoperatively stress incontinent women reported cure or improvement of their stress incontinence at the one year follow-up. As the transobturator mesh behaves like an oversized trigonal sling, it may similarly exert some limited compressive effect on the urethra and may contribute to improvement of stress urinary incontinence. A retrospective cohort study with transobturator mesh repair in women with cystocele showed that a narrower distance between the symphysis pubis and mesh on ultrasound was associated with improvement or cure of SUI.(129)

The present study adds to the growing body of evidence suggesting that prolapse surgery using trocar guided transvaginal mesh kits is associated with postoperative stress urinary incontinence. It has been hypothesised that the overall effective anterior vaginal wall and bladder neck suspension after trocar guided transvaginal mesh surgery increases the risk for postoperative stress urinary incontinence by distorting urethral pressure dynamics. (92, 130, 131) Indirect evidence to support this notion was provided by patients with point Ba inside the hymen after surgery. In this group of patients there was no significant change in stress related symptoms postoperatively. However, in women with point Ba at the hymen or beyond, improvements in stress urinary incontinence symptoms were seen postoperatively, albeit with borderline significance ($p=0.05$). This suggests that an effective elevation, or straightening, of the anterior vaginal wall and bladder neck may introduce a risk for stress urinary incontinence after transvaginal mesh surgery using a trocar guided transobturator approach.
In the present study we used the hymen to discriminate symptoms in relation to the anatomical outcome. Previous epidemiological investigations indicate that the hymen (0-plane) is an important "cut-off" level with regard to symptoms. Several studies have shown that women with prolapse beyond the hymen have more pelvic floor symptoms and are more likely to report a vaginal bulge than women with prolapse above the hymen. (12, 20, 37, 132, 133)

Strengths of this study include the prospective data collection, the multicenter study design, and the use of a standardised surgical technique using a single identical mesh

kit throughout all participating centres. The few concomitant surgical procedures add to the internal validity of our study. Among the limitations of the study we acknowledge that the lack of objective measures of lower urinary tract function and an independent control group could have provided relevant information on lower urinary tract function in relation to transvaginal mesh surgery.

By using the full range of the UDI and its subscales, we could show that trocar guided transvaginal mesh repair of anterior vaginal wall prolapse not only was associated with negative, but also positive effects with regard to both obstructive and irritative lower urinary tract symptoms. We can only speculate on the mechanisms responsible for irritative symptom relief after surgery but these effects are plausibly related to the concurrent resolution of obstructive symptoms where we observed the proportionally greatest improvements. The effect on urge urinary incontinence symptoms after prolapse surgery is limited and inconclusive. (53) Both improvement in overactive bladder symptoms (134, 135)and no changes have been reported. (136) The integral theory by Papa Petros and Ulmsten hypothesized that stress and urge symptoms both derive, for different reasons, from anatomic laxity of the anterior vaginal wall. (137)The laxity may be caused by defects in the vaginal wall itself or in the ligaments and muscles that support it. According to this theory, the vaginal wall has a structural function that prevents urgency by supporting hypothesized stretch receptors located in the proximal urethra and bladder neck. (137) It is feasible that overactive bladder symptoms are to some extent a result of bladder outlet obstruction in women with anterior vaginal wall prolapse. Altered properties of the detrusor myocytes as a result of bladder emptying difficulties caused by loss of support to the bladder, may give rise to increased excitability and activity of the detrusor muscle. (138) As a consequence, overactive bladder symptoms may decrease in parallel with improved bladder emptying following the successful restoration of anterior vaginal wall and bladder support.

9.3 Paper III

In this study, use of a trocar guided transvaginal mesh kit for anterior vaginal wall prolapse repair resulted in significantly improved anatomical outcomes with regard to lateral defects compared to anterior colporraphy. This is hardly surprising and can easily be explained since the mesh covers and supports the central and lateral anterior vaginal wall in contrast to anterior colporraphy where the midline plication only corrects a midline defect. For this reason it is interesting to note that although the anatomical results of colporraphy were inferior to the mesh group, patients in the colporraphy group nonetheless had successful correction of lateral defects in two thirds of the cases. The reason for this cannot be attributed to the effects of other procedures because no concurrent surgery was permitted at the time of study treatment. Perhaps anterior colporraphy, by reducing the surface area of the exposed vagina, brings the anterior wall back into contact with the posterior vaginal wall and reduces the tension at the ATFP junction. (47) Another possibility is that the scar tissue developed after anterior colporraphy with midline plication of the pubocervical fascia lessens the tension and thus resolves and masks the lateral defect.

In 1909 George R. White described a method of cystocele repair that consisted of "suturing the lateral sulci of the vagina to the white line of pelvic fascia" through a

vaginal approach. He was the first to describe lateral (paravaginal) defect as a cause for anterior vaginal wall prolapse. (139) In 1976 Richardson et al. reintroduced the lateral defect repair but described a technique of repair with an abdominal approach. (140) They characterized anterior wall prolapse as: lateral defects; transverse defects where the anterior vaginal wall became detached from the cervix; and midline defects where the vaginal wall itself failed. On the basis of a large series of surgical patients they concluded that most cystoceles resulted from a detachment of the pubocervical fascia at or near its lateral attachment to the ATFP. (140, 141) Although this anatomical defect is well described in the literature, the prevalence among women with anterior wall prolapse varies greatly (ranging from 37% to 88%) and the ability to diagnose these defects both pre- and intraoperative is uncertain. (47, 141-143) The prevalence of lateral defects among the examined patients in our study was in the lower range of what previously has been described (33%). Previous studies assessing the occurrence of lateral defects were, however, mainly designed and focused on determining the prevalence of lateral defects in a given population, which might have yielded a higher detection rate as compared to our study, where the diagnosis of a lateral defect was a secondary outcome measure. Also, differences in diagnostic criteria and methods between our study and previous works may contribute to the rather large discrepancy in prevalence estimates.

There is a strong association between apical descent and cystocele and the loss of apical support may contribute to the development of lateral defects. (144) In the main trial the preoperative median position of the apical segment (POP-Q point C) was within the normal range and the study population both in the main trial and this subanalysis therefore represents women that have a cystocele but no clinically significant apical descent. (90) In a retrospective chart review performed by Barber et al., the investigators reported good sensitivity and negative predictive values, but poor specificity and positive predictive values when comparing surgical findings with the preoperative clinical assessment of lateral defects (141) Dietz et al. found poor correlations between clinical examination and ultrasound imaging of lateral defects and concluded that lateral defects may be uncommon or clinically irrelevant. (145) On the other hand, De Lancey et al. found convincing support for the notion that lateral defects indeed exist when comparing women with anterior prolapse and women with normal vaginal topography at pelvic MRI. The study showed that the lateral vagina is displaced from its normal position in women with anterior prolapse (lateral defects) and was greater than changes in vaginal width (central defects) indicating that there are changes in *both* regions of the vagina. (146)

Subjective outcomes in the context of surgical repair of lateral defects are poorly investigated and described. We found that despite the large difference between the treatment groups with regard to anatomical outcomes, both at the midline and laterally, there were no significant differences between the treatment groups neither with regard to the overall UDI nor any of the UDI subscales. In agreement with Morse et al. (147) our data suggest that restoration of support at the ATFP junction does not necessarily reflect improved subjective outcomes. On the other hand we found that among patients in the colporraphy group with persistent lateral defects at the one year follow-up, only obstructive symptoms decreased significantly upon successful repair of the lateral defect. When we compared patients with anatomical failures (point Ba≥0) with non-

failures in the colporraphy group, the subscales of the UDI did not differ significantly. Although this study population was relatively small, our findings indicate that a persistent lateral defect to a greater extent influence obstructive symptoms as compared to a persistent midline weakness.

Strengths of our study include the standardized and uniform surgical procedures, use of condition specific symptom questionnaires and the POP-Q. The clinical definition we used to define lateral defects is not part of the POP-Q system, which does not include any measurement point for lateral defects, but at present there is no clinically validated method to determine if a lateral defect is present or not. (148) Another limitation is that only 78% of the randomized patients in the study were examined for lateral defects, which to some extent may be a result of selection or ascertainment bias. However, patients who were not examined for lateral defects at baseline or postoperatively did not differ from those who were examined in any significant way regarding other clinical characteristics, suggesting that the magnitude of this potential source of bias was limited.

9.4 Paper IV

Variables significantly associated with the presence of a lateral defect included previous anterior prolapse repair and HRT use. An association between HRT and gross anatomical changes such as lateral defects has not been studied previously although a theoretical link between HRT and collagen degradation has been described. (149) Furthermore, HRT has been shown to actually increase the risk for urinary incontinence in a placebo controlled RCT. (150) Thus, current evidence suggest that HRT may influence pelvic floor connective tissue resilience and support. The reason for HRT use being of particular importance for the development of lateral defects in specific remains elusive. However, one may speculate that the vaginal ATFP junction for some reason may be more sensitive to hormonal effects on collagen degradation or may increase loose connective tissue. (149) These findings should be interpreted with caution since we were unable to categorise hormone use further and as such our data should be considered as a hypothesis generating finding which is in need of corroboration and further studies.

The association between lateral defects and previous anterior prolapse repair may be an effect of the scar tissue developed after anterior colporraphy with midline plication of the pubocervical fascia lessens the tension and thus resolves and masks the lateral defect which is consistent with our previous findings in paper III and this has recently been discussed in the literature. (146) In the univariable regression model this was not significant but in the adjusted model previous anterior vaginal wall surgery decreased the odds for having a lateral defect. Considering that this factor was non-significant in univariable analysis, and the relatively small number of cases, care should be taken not to overstate conclusions from this finding because of limited statistical precision. None of the other variables included in the risk analysis showed any association with the diagnosis of a lateral defect. Richardson et al reported that lateral defects usually results in mild cystocele (140) which is in contrast with our and others findings showing no association between stage of prolapse and lateral defects. (143)

One of the main drawbacks of the present study involves classification of lateral defects. There were many physicians performing the clinical examinations, each with different experience of diagnosing lateral defects. Presumably it takes experience before becoming proficient in detecting a lateral defect, and the level of training may have influenced our detection rate. Thus classification bias may to some extent have affected our results and there is evidence suggesting that the clinical examination of anterior vaginal wall support defects displays poor inter- and intra-examiner agreement. (141) Also, there is no uniform clinical classification system or examination technique used to describe lateral defects.

With regard to subjective outcomes, patients with lateral defects were primarily characterized by an increased sensation of vaginal bulging when compared to patients with isolated central defects. No other symptoms were more commonly prevalent in the group of patients with lateral defects compared to those with a central defect only. This suggests that screening of patients using symptom surveys may not be a useful tool for the differentiation between central defects with or without concurrent lateral defects.
Current knowledge on the presentation and clinical characteristics of patients with lateral defects is rare. Our analysis also provides an opportunity for future prospective evaluations on how symptoms progress over time in relation to the occurrence and treatment of lateral defects.

It is widely assumed that obstetrical injury to pelvic floor supportive tissue structures is the most important risk factor for anterior vaginal wall prolapse. (23, 24) We recognize that it would have been of interest if more detailed information on obstetric events were included in the present analysis. Factors such as forceps delivery, external pressure and prolonged duration of labour may be relevant for the presentation of lateral defects when compared to patients only presenting with a central defect. (24, 151) Given that the number of childbirths did not differ between patients with a central and those with a lateral defect it is likely that the importance of obstetric event for the development of lateral defects needs further dissection to provide meaningful result.

10 CONCLUSIONS

The specific aims are repeated with the conclusions for the convenience of the reader:

Aim: To investigate the urodynamic effects of anterior vaginal wall prolapse surgery using either trocar guided transvaginal mesh or colporraphy. (Paper I)

Conclusion: Use of a standardized trocar-guided transvaginal mesh kit for anterior vaginal wall prolapse repair was associated with more pronounced adverse effects on maximal urethral closing pressure and a significantly increased number of women with de novo stress urinary incontinence when compared to anterior colporraphy.

Aim: To assess the effects of trocar guided transvaginal mesh on lower urinary tract symptoms after anterior vaginal wall prolapse repair. (Paper II)

Conclusion: Use of a trocar guided transvaginal mesh kit for anterior vaginal wall prolapse repair was associated with an overall resolution of most symptoms associated with urge urinary incontinence and bladder outlet obstruction. These beneficial effects should be weighed against the increased risk for stress urinary incontinence related to the procedure.

Aim: To evaluate objective and subjective outcomes following the use of transvaginal mesh compared with traditional colporraphy for repair of anterior vaginal wall lateral defects. (Paper III)

Conclusion: Trocar guided transvaginal mesh kit significantly improved the odds for restoration of lateral vaginal support and vaginal topography in patients with lateral defects as compared to traditional anterior colporraphy. However, this did not result in significant differences in patient reported outcomes after one year.

Aim: To compare clinical characteristics and symptoms among patients with isolated central defects and patients with a combination of both central and lateral defects. (Paper IV)

Conclusion: Clinical patient characteristics has a limited role in the occurrence of lateral defects among patients with anterior vaginal wall prolapse and most subjective symptoms are shared with isolated central anterior vaginal wall prolapse.

11 POPULÄRVETENSKAPLIG SAMMANFATTNING

Svaghet i bäckenbotten i form av framfall medför att slidans väggar buktar eller att livmodern faller ner och kan ge olika symtom hos kvinnor. Det vanligaste symtomet, och som oftast är orsaken till att kvinnan söker sjukvård, är känslan av att något faller fram i slidan (globuskänsla). Efter vaginal förlossning uppvisar nära hälften av alla kvinnor anatomiska fynd på grund av bristande stöd för slidväggarna. Alla dessa kvinnor har dock inte symtom. Riskfaktorer för bäckenbottensvaghet anses vara: många graviditeter, svåra förlossningar, ökad ålder och övervikt. Framfallsoperationer tillhör en av de vanligaste gynekologiska operationerna och det utförs ca 8000 operationer i Sverige varje år. Ett ökat sjukvårdsbehov kan väntas när kvinnor blir allt äldre. Någon säkerställd profylax finns inte.

De operationsmetoder som använts i över hundra år har i studier visats sig ge stor risk för återfall och är sparsamt utvärderade. Otillfredsställande resultat efter operation är vanliga. Vid traditionell kirurgi av framfall försöker man återskapa anatomin genom att förstärka den skadade vävnaden med olika suturer. Uppskattningsvis får var tredje kvinna som opereras ett återfall. Operationsmetoder med användande av syntetiska nät har under de senaste åren prövats med varierande resultat. Vid ljumskbråckskirurgi och urininkontinenskirurgi har man uppnått goda operationsresultat vid användning av syntetiska polypropylennät som stöd för den sviktande vävnaden och till följd av detta sker en ökad användning av syntetiska implantat även vid framfallskirurgi. Användandet ökar nu snabbt baserat på rapporter om förbättrade resultat och färre återfall. Dock förefaller de nya metoderna medföra ökad risk för komplikationer och långtidsresultat saknas. Det är därför viktigt att fortsatt utvärdera dessa metoder. Denna avhandling avser belysa kliniska aspekter, såväl anatomiska som subjektiva utfall vid framfallsoperationer av främre vaginalväggen med syntetiska nät.

I den första studien har fem kliniker i Sverige och Danmark samarbetat i en randomiserad kontrollerad studie. 52 kvinnor med framfall i främre vaginalväggen lottades till traditionell kirurgi eller operation med ett syntetiskt nät. Nätet placerades med hjälp av metalledare för att åtgärda framfallet. De undersöktes gynekologiskt och fick fylla i enkäter angående symtom av framfall och urinbesvär före operationen och 2 månader efter. Patienterna fick även genomgå urodynamisk undersökning som avser utreda funktionen av urinblåsan och urinröret. Vi fann en ökad förekomst av ofrivilligt urinläckage i samband med hostprovokation hos patienterna som opererats med nät jämfört med de kvinnor som opererats med traditionell metod.

I den andra studien har flera kliniker i de nordiska länderna samarbetat i en prospektiv kohortstudie. 109 kvinnor med framfall i framväggen inkluderades och genomgick operation med ett syntetiskt nät. Ett validerat frågeformulär med 19 frågor om framfallsrelaterade besvär fylldes i före operation och efter ett år. Uppgivna symtom från urinblåsan och urinröret såsom urinträngningar, trängningsinkontinens och blåstömningsbesvär förbättrades. Känslan av att något buktar ut ur slidan (globuskänsla), tyngdkänsla och smärta i bäckenet förbättrades också efter operationen. Kvinnorna förbättrades dock inte beträffande symtom som rörde ansträngningsinkontinens och 11% fick nytillkommen ansträngningsinkontinens.

I den tredje studien har vi ur en stor, randomiserad multicenterstudie utvärderat två olika operationsmetoders effekt på de anatomiska strukturerna i vaginas framvägg och symtom. 99 patienter med s.k. laterala defekter inkluderades och vi fann att nätoperation i framväggen korrigerade laterala defekterna i signifikant högre utsträckning än traditionell kirurgi ett år efter operation. Vid traditionell kirurgi korrigerar man bara defekter i medellinjen medan man vid nätoperationen täcker hela främre vaginalväggen. Trots detta fann vi ingen skillnad i symtom mellan grupperna.

Den fjärde studien är en tvärsnittsstudie och använder sig av samma patientgrupp som den stora randomiserade multicenterstudien och fokuserar på att jämföra faktorer som kan tänkas påverka/ha betydelse för lateral defekt. 203 kvinnor utan lateral defekt jämfördes med 99 kvinnor med lateral defekt avseende kliniska karakteristika och vi fann att användandet av hormoner i samband med klimakteriet ökade risken för lateral defekt och kvinnor som tidigare i livet genomgått framfallsoperation av framväggen hade lägre risk för att ha lateral defekt.

I denna avhandling har vi funnit att standardiserade framfallsoperationer med nät kan genomföras med tillfredställande subjektiva och anatomiska resultat. Det föreligger dock en ökad risk för besvär med ansträngningsinkontinens efter operationen. I jämförelse med den traditionella kirurgin är operationer med syntetiska nät fortfarande en ny metod där potentiella risker och vinster, framförallt på lång sikt, måste övervägas.

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13 REFERENCES

1. Jelovsek, J.E., C. Maher, and M.D. Barber, *Pelvic organ prolapse.* Lancet, 2007. **369**(9566): p. 1027-38.
2. Jelovsek, J.E. and M.D. Barber, *Women seeking treatment for advanced pelvic organ prolapse have decreased body image and quality of life.* Am J Obstet Gynecol, 2006. **194**(5): p. 1455-61.
3. Miedel, A., et al., *Symptoms and pelvic support defects in specific compartments.* Obstet Gynecol, 2008. **112**(4): p. 851-8.
4. Sand, P.K., et al., *Prospective randomized trial of polyglactin 910 mesh to prevent recurrence of cystoceles and rectoceles.* Am J Obstet Gynecol, 2001. **184**(7): p. 1357-62; discussion 1362-4.
5. Weber, A.M., et al., *Anterior colporrhaphy: a randomized trial of three surgical techniques.* Am J Obstet Gynecol, 2001. **185**(6): p. 1299-304;.
6. Ashton-Miller, J.A. and J.O. DeLancey, *Functional anatomy of the female pelvic floor.* Ann N Y Acad Sci, 2007. **1101**: p. 266-96.
7. Heesakkers, J.P. and R.R. Gerretsen, *Urinary incontinence: sphincter functioning from a urological perspective.* Digestion, 2004. **69**(2): p. 93-101.
8. Delancey, J.O., *Why do women have stress urinary incontinence?* Neurourol Urodyn, 2010. **29 1**: p. S13-7.
9. DeLancey, J.O., *Anatomic aspects of vaginal eversion after hysterectomy.* Am J Obstet Gynecol, 1992. **166**(6 Pt 1): p. 1717-28.
10. Whinters, C., in *ICS*. 2011.
11. Tegerstedt, G., et al., *Prevalence of symptomatic pelvic organ prolapse in a Swedish population.* Int Urogynecol J Pelvic Floor Dysfunct, 2005. **16**(6): p. 497-503.
12. Swift, S., et al., *Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects.* Am J Obstet Gynecol, 2005. **192**(3): p. 795-806.
13. Samuelsson, E.C., et al., *Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors.* Am J Obstet Gynecol, 1999. **180**(2 Pt 1): p. 299-305.
14. Uustal Fornell, E., G. Wingren, and P. Kjolhede, *Factors associated with pelvic floor dysfunction with emphasis on urinary and fecal incontinence and genital prolapse: an epidemiological study.* Acta Obstet Gynecol Scand, 2004. **83**(4): p. 383-9.
15. Olsen, A.L., et al., *Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence.* Obstet Gynecol, 1997. **89**(4): p. 501-6.
16. Brown, J.S., et al., *Pelvic organ prolapse surgery in the United States, 1997.* Am J Obstet Gynecol, 2002. **186**(4): p. 712-6.
17. Clark, A.L., et al., *Epidemiologic evaluation of reoperation for surgically treated pelvic organ prolapse and urinary incontinence.* Am J Obstet Gynecol, 2003. **189**(5): p. 1261-7.
18. Miedel, A., et al., *A 5-year prospective follow-up study of vaginal surgery for pelvic organ prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2008. **19**(12): p. 1593-601.
19. Dietz, H.P., *The aetiology of prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2008. **19**(10): p. 1323-9.
20. Miedel, A., et al., *Nonobstetric risk factors for symptomatic pelvic organ prolapse.* Obstet Gynecol, 2009. **113**(5): p. 1089-97.

21. Mant, J., R. Painter, and M. Vessey, *Epidemiology of genital prolapse: observations from the Oxford Family Planning Association Study.* Br J Obstet Gynaecol, 1997. **104**(5): p. 579-85.
22. Rortveit, G., et al., *Age- and type-dependent effects of parity on urinary incontinence: the Norwegian EPINCONT study.* Obstet Gynecol, 2001. **98**(6): p. 1004-10.
23. Tegerstedt, G., et al., *Obstetric risk factors for symptomatic prolapse: a population-based approach.* Am J Obstet Gynecol, 2006. **194**(1): p. 75-81.
24. DeLancey, J.O., et al., *The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery.* Obstet Gynecol, 2003. **101**(1): p. 46-53.
25. Dietz, H.P. and V. Lanzarone, *Levator trauma after vaginal delivery.* Obstet Gynecol, 2005. **106**(4): p. 707-12.
26. DeLancey, J.O., et al., *Vaginal birth and de novo stress incontinence: relative contributions of urethral dysfunction and mobility.* Obstet Gynecol, 2007. **110**(2 Pt 1): p. 354-62.
27. DeLancey, J.O., et al., *Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse.* Obstet Gynecol, 2007. **109**(2 Pt 1): p. 295-302.
28. Hoyte, L., et al., *Two- and 3-dimensional MRI comparison of levator ani structure, volume, and integrity in women with stress incontinence and prolapse.* Am J Obstet Gynecol, 2001. **185**(1): p. 11-9.
29. Jorgensen, S., H.O. Hein, and F. Gyntelberg, *Heavy lifting at work and risk of genital prolapse and herniated lumbar disc in assistant nurses.* Occup Med 1994. **44**(1): p. 47-9.
30. Spence-Jones, C., et al., *Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence.* Br J Obstet Gynaecol, 1994. **101**(2): p. 147-52.
31. Altman, D., et al., *Genetic influence on stress urinary incontinence and pelvic organ prolapse.* Eur Urol, 2008. **54**(4): p. 918-22.
32. Forsgren, C., et al., *Risk factors for vaginal vault prolapse surgery in postmenopausal hysterectomized women.* Menopause, 2008. **15**(6): p. 1115-9.
33. Chen, B.H., et al., *Collagen metabolism and turnover in women with stress urinary incontinence and pelvic prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2002. **13**(2): p. 80-7
34. Soderberg, M.W., et al., *Young women with genital prolapse have a low collagen concentration.* Acta Obstet Gynecol Scand, 2004. **83**(12): p. 1193-8.
35. Ellerkmann, R.M., et al., *Correlation of symptoms with location and severity of pelvic organ prolapse.* Am J Obstet Gynecol, 2001. **185**(6): p. 1332-7;
36. Tegerstedt, G., et al., *A short-form questionnaire identified genital organ prolapse.* J Clin Epidemiol, 2005. **58**(1): p. 41-6.
37. Swift, S.E., S.B. Tate, and J. Nicholas, *Correlation of symptoms with degree of pelvic organ support in a general population of women: what is pelvic organ prolapse?* Am J Obstet Gynecol, 2003. **189**(2): p. 372-7;
38. Barber, M.D., et al., *Defining success after surgery for pelvic organ prolapse.* Obstet Gynecol, 2009. **114**(3): p. 600-9.
39. Burrows, L.J., et al., *Pelvic symptoms in women with pelvic organ prolapse.* Obstet Gynecol, 2004. **104**(5 Pt 1): p. 982-8.
40. Barber, M.D., *Symptoms and outcome measures of pelvic organ prolapse.* Clin Obstet Gynecol, 2005. **48**(3): p. 648-61.

41. Abrams, P., et al., *The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society.* Neurourol Urodyn, 2002. **21**(2): p. 167-78.
42. Serati, M., et al., *Urinary symptoms and urodynamic findings in women with pelvic organ prolapse: is there a correlation? Results of an artificial neural network analysis.* Eur Urol, 2011. **60**(2): p. 253-60.
43. Mouritsen, L., *Classification and evaluation of prolapse.* Best Pract Res Clin Obstet Gynaecol, 2005. **19**(6): p. 895-911.
44. Romanzi, L.J., D.C. Chaikin, and J.G. Blaivas, *The effect of genital prolapse on voiding.* J Urol, 1999. **161**(2): p. 581-6.
45. Richardson, A.C., P.B. Edmonds, and N.L. Williams, *Treatment of stress urinary incontinence due to paravaginal fascial defect.* Obstet Gynecol, 1981. **57**(3): p. 357-62.
46. DeLancey, J.O., *Structural support of the urethra as it relates to stress urinary incontinence: the hammock hypothesis.* Am J Obstet Gynecol, 1994. **170**(6): p. 1713-20
47. Delancey, J.O., *Fascial and muscular abnormalities in women with urethral hypermobility and anterior vaginal wall prolapse.* Am J Obstet Gynecol, 2002. **187**(1): p. 93-8.
48. Richardson, D.A., A.E. Bent, and D.R. Ostergard, *The effect of uterovaginal prolapse on urethrovesical pressure dynamics.* Am J Obstet Gynecol, 1983. **146**(8): p. 901-5.
49. Liang, C.C., et al., *Pessary test to predict postoperative urinary incontinence in women undergoing hysterectomy for prolapse.* Obstet Gynecol, 2004. **104**(4): p. 795-800.
50. Reena, C., A.N. Kekre, and N. Kekre, *Occult stress incontinence in women with pelvic organ prolapse.* Int J Gynaecol Obstet, 2007. **97**(1): p. 31-4.
51. Visco, A.G., et al., *The role of preoperative urodynamic testing in stress-continent women undergoing sacrocolpopexy: the Colpopexy and Urinary Reduction Efforts (CARE) randomized surgical trial.* Int Urogynecol J Pelvic Floor Dysfunct, 2008. **19**(5): p. 607-14.
52. de Tayrac, R., et al., *Combined genital prolapse repair reinforced with a polypropylene mesh and tension-free vaginal tape in women with genital prolapse and stress urinary incontinence: a retrospective case-control study with short-term follow-up.* Acta Obstet Gynecol Scand, 2004. **83**(10): p. 950-4.
53. Maher, C.M., et al., *Surgical management of pelvic organ prolapse in women: the updated summary version Cochrane review.* Int Urogynecol J, 2011. **22**(11): p. 1445-57.
54. Chaikin, D.C., A. Groutz, and J.G. Blaivas, *Predicting the need for anti-incontinence surgery in continent women undergoing repair of severe urogenital prolapse.* J Urol, 2000. **163**(2): p. 531-4.
55. Rosenzweig, B.A., et al., *Prevalence of abnormal urodynamic test results in continent women with severe genitourinary prolapse.* Obstet Gynecol, 1992. **79**(4): p. 539-42.
56. Gallentine, M.L. and R.D. Cespedes, *Occult stress urinary incontinence and the effect of vaginal vault prolapse on abdominal leak point pressures.* Urology, 2001. **57**(1): p. 40-4.
57. Romanzi, L.J., *Management of the urethral outlet in patients with severe prolapse.* Curr Opin Urol, 2002. **12**(4): p. 339-44.
58. Veronikis, D.K., D.H. Nichols, and M.M. Wakamatsu, *The incidence of low-pressure urethra as a function of prolapse-reducing technique in patients with*

massive pelvic organ prolapse (maximum descent at all vaginal sites). Am J Obstet Gynecol, 1997. **177**(6): p. 1305-13
59. Bump, R.C., J.A. Fantl, and W.G. Hurt, *The mechanism of urinary continence in women with severe uterovaginal prolapse: results of barrier studies.* Obstet Gynecol, 1988. **72**(3 Pt 1): p. 291-5.
60. Meschia, M., et al., *A randomized comparison of tension-free vaginal tape and endopelvic fascia plication in women with genital prolapse and occult stress urinary incontinence.* Am J Obstet Gynecol, 2004. **190**(3): p. 609-13.
61. Wall, L.L. and J.K. Hewitt, *Urodynamic characteristics of women with complete posthysterectomy vaginal vault prolapse.* Urology, 1994. **44**(3): p. 336-41
62. Roovers, J.P. and M. Oelke, *Clinical relevance of urodynamic investigation tests prior to surgical correction of genital prolapse: a literature review.* Int Urogynecol J Pelvic Floor Dysfunct, 2007. **18**(4): p. 455-60.
63. Carter, P.G., P. Lewis, and P. Abrams, *Urodynamic morbidity and dysuria prophylaxis.* Br J Urol, 1991. **67**(1): p. 40-1.
64. Okorocha, I., G. Cumming, and I. Gould, *Female urodynamics and lower urinary tract infection.* BJU Int, 2002. **89**(9): p. 863-7.
65. Weber, A.M. and M.D. Walters, *Cost-effectiveness of urodynamic testing before surgery for women with pelvic organ prolapse and stress urinary incontinence.* Am J Obstet Gynecol, 2000. **183**(6): p. 1338-46;
66. Bump, R.C., et al., *The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction.* Am J Obstet Gynecol, 1996. **175**(1): p. 10-7.
67. Swift, S., et al., *Validation of a simplified technique for using the POPQ pelvic organ prolapse classification system.* Int Urogynecol J Pelvic Floor Dysfunct, 2006. **17**(6): p. 615-20.
68. Shull, B.L., et al., *A transvaginal approach to repair of apical and other associated sites of pelvic organ prolapse with uterosacral ligaments.* Am J Obstet Gynecol, 2000. **183**(6): p. 1365-73
69. Whiteside, J.L., et al., *Risk factors for prolapse recurrence after vaginal repair.* Am J Obstet Gynecol, 2004. **191**(5): p. 1533-8.
70. Morrisroe, S., U. Lee, and S. Raz, *The use of mesh in vaginal prolapse repair: do the benefits justify the risks?* Curr Opin Urol, 2010. **20**(4): p. 275-9.
71. Chmielewski, L., et al., *Reanalysis of a randomized trial of 3 techniques of anterior colporrhaphy using clinically relevant definitions of success.* Am J Obstet Gynecol, 2011. **205**(1): p. 69 e1-8.
72. Boyles, S.H., A.M. Weber, and L. Meyn, *Procedures for pelvic organ prolapse in the United States, 1979-1997.* Am J Obstet Gynecol, 2003. **188**(1): p. 108-15.
73. Maher, C., et al., *Surgical management of pelvic organ prolapse in women.* Cochrane Database of Systematic Reviews, (4).
74. Kelly, *Incontinence of urine in women.* Urol Cutan Rev, 1913. **1**: p. 291-3.
75. Bruce, R.G., R.E. El-Galley, and N.T. Galloway, *Paravaginal defect repair in the treatment of female stress urinary incontinence and cystocele.* Urology, 1999. **54**(4): p. 647-51.
76. Julian, T.M., *The efficacy of Marlex mesh in the repair of severe, recurrent vaginal prolapse of the anterior midvaginal wall.* Am J Obstet Gynecol, 1996. **175**(6): p. 1472-5.
77. Mallipeddi, P.K., et al., *Anatomic and functional outcome of vaginal paravaginal repair in the correction of anterior vaginal wall prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2001. **12**(2): p. 83-8.

78. Young, S.B., J.J. Daman, and L.G. Bony, *Vaginal paravaginal repair: one-year outcomes.* Am J Obstet Gynecol, 2001. **185**(6): p. 1360-6.
79. Chen, C.C., B. Ridgeway, and M.F. Paraiso, *Biologic grafts and synthetic meshes in pelvic reconstructive surgery.* Clin Obstet Gynecol, 2007. **50**(2): p. 383-411.
80. Burger, J.W., et al., *Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia.* Ann Surg, 2004. **240**(4): p. 578-83.
81. Emge, L.A. and R.B. Durfee, *Pelvic organ prolapse: four thousand years of treatment.* Clin Obstet Gynecol, 1966. **9**(4): p. 997-1032.
82. Debodinance, P., et al., *[Synthetic meshes for transvaginal surgical cure of genital prolapse: evaluation in 2005]*. J Gynecol Obstet Biol Reprod (Paris), 2006. **35**(5 Pt 1): p. 429-54.
83. Foon, R. and P. Smith, *The effectiveness and complications of graft materials used in vaginal prolapse surgery.* Curr Opin Obstet Gynecol, 2009. **21**(5): p. 424-7.
84. Amid, P.K. and I.L. Lichtenstein, *[Current assessment of Lichtenstein tension-free hernia repair]*. Chirurg, 1997. **68**(10): p. 959-64.
85. Goldstein, H.S., *A university experience using mesh in inguinal hernia repair.* Hernia, 2001. **5**(4): p. 182-5.
86. Griffis, K. and D.S. Hale, *Grafts in pelvic reconstructive surgery.* Clin Obstet Gynecol, 2005. **48**(3): p. 713-23.
87. Falconer, C., et al., *Clinical outcome and changes in connective tissue metabolism after intravaginal slingplasty in stress incontinent women.* Int Urogynecol J Pelvic Floor Dysfunct, 1996. **7**(3): p. 133-7.
88. Rosch, R., et al., *Mesh implants in hernia repair. Inflammatory cell response in a rat model.* Eur Surg Res, 2003. **35**(3): p. 161-6.
89. Herschorn, S., *The use of biological and synthetic materials in vaginal surgery for prolapse.* Curr Opin Urol, 2007. **17**(6): p. 408-14.
90. Altman, D., et al., *Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse.* N Engl J Med. **364**(19): p. 1826-36.
91. Carey, M., et al., *Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial.* BJOG, 2009. **116**(10): p. 1380-6.
92. Elmer, C., et al., *Trocar-guided transvaginal mesh repair of pelvic organ prolapse.* Obstet Gynecol, 2009. **113**(1): p. 117-26.
93. Jacquetin, B., et al., *Total transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse: a 3-year prospective follow-up study.* Int Urogynecol J, 2010. **21**(12): p. 1455-62.
94. Moore, R.D., et al., *Prospective multicenter trial assessing type I, polypropylene mesh placed via transobturator route for the treatment of anterior vaginal prolapse with 2-year follow-up.* Int Urogynecol J, 2010. **21**(5): p. 545-52.
95. Nguyen, J.N. and R.J. Burchette, *Outcome after anterior vaginal prolapse repair: a randomized controlled trial.* Obstet Gynecol, 2008. **111**(4): p. 891-8.
96. Nieminen, K., et al., *Outcomes after anterior vaginal wall repair with mesh: a randomized, controlled trial with a 3 year follow-up.* Am J Obstet Gynecol, 2010. **203**(3): p. 235 e1-8.
97. Withagen, M.I., et al., *Trocar-guided mesh compared with conventional vaginal repair in recurrent prolapse: a randomized controlled trial.* Obstet Gynecol, 2011. **117**(2 Pt 1): p. 242-50.

98. Jia, X., et al., *Efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse: systematic review and meta-analysis.* BJOG, 2008. **115**(11): p. 1350-61.
99. Dennerstein, L., J.L. Alexander, and K. Kotz, *The menopause and sexual functioning: a review of the population-based studies.* Annu Rev Sex Res, 2003. **14**: p. 64-82.
100. Sobhgol, S.S. and S.M. Alizadeli Charndabee, *Rate and related factors of dyspareunia in reproductive age women: a cross-sectional study.* Int J Impot Res, 2007. **19**(1): p. 88-94.
101. Weber, A.M., M.D. Walters, and M.R. Piedmonte, *Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence.* Am J Obstet Gynecol, 2000. **182**(6): p. 1610-5.
102. Handa, V.L., et al., *Sexual function before and after sacrocolpopexy for pelvic organ prolapse.* Am J Obstet Gynecol, 2007. **197**(6): p. 629 e1-6.
103. Silva, W.A., et al., *Uterosacral ligament vault suspension: five-year outcomes.* Obstet Gynecol, 2006. **108**(2): p. 255-63.
104. Maher, C., et al., *Surgical management of pelvic organ prolapse in women: a short version Cochrane review.* Neurourol Urodyn, 2008. **27**(1): p. 3-12.
105. Fayyad, A.M., et al., *Prospective study of anterior transobturator mesh kit (Prolift) for the management of recurrent anterior vaginal wall prolapse.* Int Urogynecol J, 2011. **22**(2): p. 157-63.
106. Milani, A.L., M.I. Withagen, and M.E. Vierhout, *Trocar-guided total tension-free vaginal mesh repair of post-hysterectomy vaginal vault prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2009. **20**(10): p. 1203-11.
107. Altman, D., et al., *Sexual dysfunction after trocar-guided transvaginal mesh repair of pelvic organ prolapse.* Obstet Gynecol, 2009. **113**(1): p. 127-33.
108. Feiner, B., L. Gietelink, and C. Maher, *Anterior vaginal mesh sacrospinous hysteropexy and posterior fascial plication for anterior compartment dominated uterovaginal prolapse.* Int Urogynecol J, 2010. **21**(2): p. 203-8.
109. Aungst, M.J., et al., *De novo stress incontinence and pelvic muscle symptoms after transvaginal mesh repair.* Am J Obstet Gynecol, 2009. **201**(1): p. 73 e1-7.
110. de Landsheere, L., et al., *Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up.* Am J Obstet Gynecol, 2011.
111. Abed, H., et al., *Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review.* Int Urogynecol J, 2011. **22**(7): p. 789-98.
112. Achtari, C., et al., *Risk factors for mesh erosion after transvaginal surgery using polypropylene (Atrium) or composite polypropylene/polyglactin 910 (Vypro II) mesh.* Int Urogynecol J Pelvic Floor Dysfunct, 2005. **16**(5): p. 389-94.
113. Araco, F., G. Gravante, and E. Piccione, *Bladder erosion after 2 years from cystocele repair with type I polypropylene mesh.* Int Urogynecol J Pelvic Floor Dysfunct, 2009. **20**(6): p. 731-3.
114. Belot, F., et al., *[Risk factors for prosthesis exposure in treatment of genital prolapse via the vaginal approach]*. Gynecol Obstet Fertil, 2005. **33**(12): p. 970-4.
115. Schafer, W., et al., *Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies.* Neurourol Urodyn, 2002. **21**(3): p. 261-74.

116. Lose, G., et al., *Standardisation of urethral pressure measurement: report from the Standardisation Sub-Committee of the International Continence Society.* Neurourol Urodyn, 2002. **21**(3): p. 258-60.
117. Shumaker, S.A., et al., *Health-related quality of life measures for women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Continence Program in Women (CPW) Research Group.* Qual Life Res, 1994. **3**(5): p. 291-306.
118. Kasturi, S., et al., *De novo stress urinary incontinence after negative prolapse reduction stress testing for total vaginal mesh procedures: incidence and risk factors.* Am J Obstet Gynecol, 2011. **205**(5): p. 487 e1-4.
119. Weber, A.M., *Is urethral pressure profilometry a useful diagnostic test for stress urinary incontinence?* Obstet Gynecol Surv, 2001. **56**(11): p. 720-35.
120. Colli, E., et al., *Are urodynamic tests useful tools for the initial conservative management of non-neurogenic urinary incontinence? A review of the literature.* Eur Urol, 2003. **43**(1): p. 63-9.
121. Caruso, D.J., et al., *What is the predictive value of urodynamics to reproduce clinical findings of urinary frequency, urge urinary incontinence, and/or stress urinary incontinence?* Int Urogynecol J, 2010. **21**(10): p. 1205-9.
122. Khan, M.S., et al., *The relationship between urinary symptom questionnaires and urodynamic diagnoses: an analysis of two methods of questionnaire administration.* BJOG, 2004. **111**(5): p. 468-74.
123. Ek, M., et al., *Urodynamic assessment of anterior vaginal wall surgery: A randomized comparison between colporraphy and transvaginal mesh.* Neurourol Urodyn, 2009.
124. Hiltunen, R., et al., *Low-weight polypropylene mesh for anterior vaginal wall prolapse: a randomized controlled trial.* Obstet Gynecol, 2007. **110**(2 Pt 2): p. 455-62.
125. Iglesia, C.B., et al., *Vaginal mesh for prolapse: a randomized controlled trial.* Obstet Gynecol, 2010. **116**(2 Pt 1): p. 293-303.
126. Haylen, B.T., et al., *An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction.* Neurourol Urodyn, 2010. **29**(1): p. 4-20.
127. Sivaslioglu, A.A., E. Unlubilgin, and I. Dolen, *A randomized comparison of polypropylene mesh surgery with site-specific surgery in the treatment of cystocoele.* Int Urogynecol J Pelvic Floor Dysfunct, 2008. **19**(4): p. 467-71.
128. Moore, R.D. and J.R. Miklos, *Vaginal repair of cystocele with anterior wall mesh via transobturator route: efficacy and complications with up to 3-year followup.* Adv Urol, 2009: p. 743831.
129. Shek, K.L., et al., *Stress urinary incontinence after transobturator mesh for cystocele repair.* Int Urogynecol J Pelvic Floor Dysfunct, 2009. **20**(4): p. 421-5.
130. Fatton, B., et al., *Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolift technique)--a case series multicentric study.* Int Urogynecol J Pelvic Floor Dysfunct, 2007. **18**(7): p. 743-52.
131. van Raalte, H.M., et al., *One-year anatomic and quality-of-life outcomes after the Prolift procedure for treatment of posthysterectomy prolapse.* Am J Obstet Gynecol, 2008. **199**(6): p. 694 e1-6.
132. Bradley, C.S. and I.E. Nygaard, *Vaginal wall descensus and pelvic floor symptoms in older women.* Obstet Gynecol, 2005. **106**(4): p. 759-66.
133. Mouritsen, L. and J.P. Larsen, *Symptoms, bother and POPQ in women referred with pelvic organ prolapse.* Int Urogynecol J Pelvic Floor Dysfunct, 2003. **14**(2): p. 122-7.

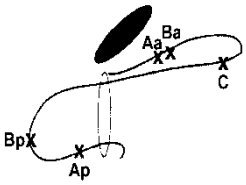
134. Digesu, G.A., et al., *Do overactive bladder symptoms improve after repair of anterior vaginal wall prolapse?* Int Urogynecol J Pelvic Floor Dysfunct, 2007. **18**(12): p. 1439-43.
135. Nguyen, J.K. and N.N. Bhatia, *Resolution of motor urge incontinence after surgical repair of pelvic organ prolapse.* J Urol, 2001. **166**(6): p. 2263-6.
136. Milani, R., et al., *Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh.* BJOG, 2005. **112**(1): p. 107-11.
137. Petros, P.E. and U.I. Ulmsten, *An integral theory of female urinary incontinence. Experimental and clinical considerations.* Acta Obstet Gynecol Scand Suppl, 1990. **153**: p. 7-31.
138. Brading, A.F., *A myogenic basis for the overactive bladder.* Urology, 1997. **50**(6A Suppl): p. 57-67.
139. White, A., *Cystocele.* JAMA, 1909. **21**: p. 1707-1710.
140. Richardson, A.C., J.B. Lyon, and N.L. Williams, *A new look at pelvic relaxation.* Am J Obstet Gynecol, 1976. **126**(5): p. 568-73.
141. Barber, M.D., et al., *Accuracy of clinical assessment of paravaginal defects in women with anterior vaginal wall prolapse.* Am J Obstet Gynecol, 1999. **181**(1): p. 87-90.
142. Nguyen, J.K., *Current concepts in the diagnosis and surgical repair of anterior vaginal prolapse due to paravaginal defects.* Obstet Gynecol Surv, 2001. **56**(4): p. 239-46.
143. Segal, J.L., et al., *Paravaginal defects: prevalence and accuracy of preoperative detection.* Int Urogynecol J Pelvic Floor Dysfunct, 2004. **15**(6): p. 378-83.
144. Summers, A., et al., *The relationship between anterior and apical compartment support.* Am J Obstet Gynecol, 2006. **194**(5): p. 1438-43.
145. Dietz, H.P., et al., *Paravaginal defects: a comparison of clinical examination and 2D/3D ultrasound imaging.* Aust N Z J Obstet Gynaecol, 2005. **45**(3): p. 187-90.
146. Larson, K.A., et al., *3D analysis of cystoceles using magnetic resonance imaging assessing midline, paravaginal, and apical defects.* Int Urogynecol J, 2012. **23**(3): p. 285-93.
147. Morse, A.N., et al., *Midline anterior repair alone vs anterior repair plus vaginal paravaginal repair: a comparison of anatomic and quality of life outcomes.* Int Urogynecol J Pelvic Floor Dysfunct, 2007. **18**(3): p. 245-9.
148. Whiteside, J.L., et al., *Clinical evaluation of anterior vaginal wall support defects: interexaminer and intraexaminer reliability.* Am J Obstet Gynecol, 2004. **191**(1): p. 100-4.
149. Jackson, R.A., et al., *Urinary incontinence in elderly women: findings from the Health, Aging, and Body Composition Study.* Obstet Gynecol, 2004. **104**(2): p. 301-7.
150. Hendrix, S.L., et al., *Effects of estrogen with and without progestin on urinary incontinence.* JAMA, 2005. **293**(8): p. 935-48.
151. Kearney, R., et al., *Obstetric factors associated with levator ani muscle injury after vaginal birth.* Obstet Gynecol, 2006. **107**(1): p. 144-9.

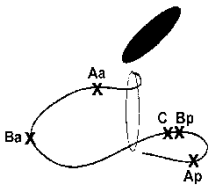
14 APPENDIX

14.1 POP-Q protocol paper I-IV

POP-Q kvantifiering enligt ICS-standardisation committee.

A	**BA**	**C**
gh	**P**	**tvl**
Ap	**Bp**	**D**





Anser du att det föreligger en lateral sänkning av vaginalväggen (lateral defekt):

□ Ja □ Nej

14.2 Urodynamic protocol paper I

Urodynamisk us TVM III

Tilldelat randomiseringsnummer……
Datum för undersökning……
Sjukhus……

Preoperativ us ☐ Postoperativ us ☐

1. Mätning av resurin (ml) ☐
2. Maximal cystometrisk blåskapacitet (ml) ☐

	Ja	Nej
3. Detrusor kontraktioner under fyllnadsfasen	☐	☐

4. Lätta trängningar vid Volym……
5. Starka trängningar vid Volym……
6. Avtappning av blåsan till 300 ml
7. Urethratryckprofiler MUCP (maximum urethral closing pressure) ……cm H2O

	Ja	Nej
8. Hostläckage vid hostprovokation med kateter borttagen (ca 300 ml i blåsan)	☐	☐

9. Q-max (flödesmätning) …… (ml/s)
10. Resurin ……(ml)

14.3 Questionnaire paper II-IV, UDI original form.

Följande frågor avser att undersöka i vilken utsträckning du upplever symptom från bäckenbotten och nedre urinvägarna:

	Nej	**Om Ja, hur mycket besvärar det Dig?**			
		Inte alls	Lite	Måttligt	Mycket
Upplever du att du kissar ofta?	□	□	□	□	□
Har du stark känsla av urinträngning?	□	□	□	□	□
Upplever du urinläckage vid trängning?	□	□	□	□	□
Läcker det urin vid fysisk ansträngning, hosta?	□	□	□	□	□
Läcker urin utan relation till aktivitet?	□	□	□	□	□
Läcker det urin droppvis?	□	□	□	□	□
Läcker det stora mängder urin?	□	□	□	□	□
Går du upp på natten för att kissa?	□	□	□	□	□
Upplever du sängvätning?	□	□	□	□	□
Upplever du svårigheter att tömma blåsan?	□	□	□	□	□
Kan det kännas som om blåsan inte är tömd?	□	□	□	□	□
Upplever du ett tryck i nedre delen av buken?	□	□	□	□	□
Kan det göra ont när du kissar?	□	□	□	□	□
Har du värk i underlivet?	□	□	□	□	□
Har du tyngdkänsla i underlivet?	□	□	□	□	□
Känns det som om något buktar i underlivet?	□	□	□	□	□
Erfar du obehag i underlivet i stående eller vid fysisk ansträngning?	□	□	□	□	□
Måste du trycka i slidan för att tömma tarmen?	□	□	□	□	□